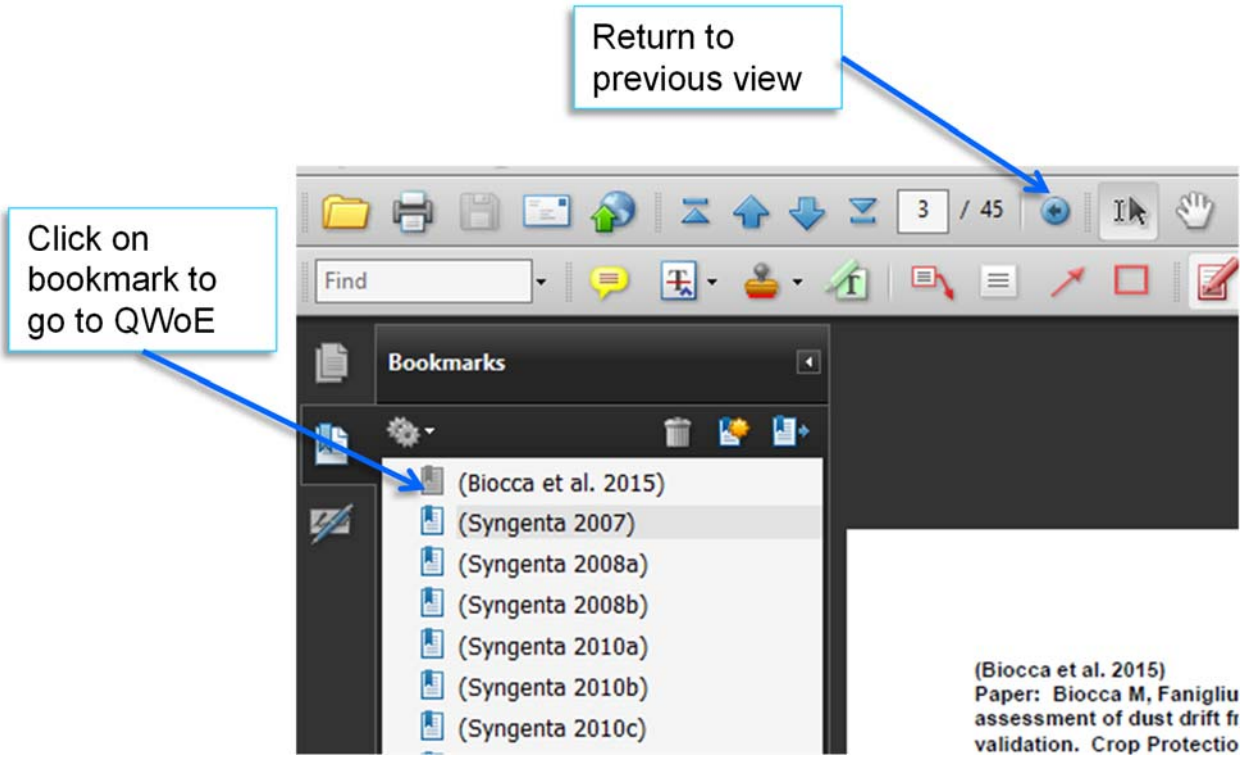
Supplemental information

Supplemental information for Stephenson & Solomon. 2017. Weight of evidence assessment of higher tier studies on the toxicity and risks of neonicotinoids in honeybees. 4. Thiamethoxam.

The following are the QWoE evaluations for the studies used in the analysis. This SI is a complete description of the WoE analysis of the papers and reports used in the paper. This is an Adobe PDF file and can be fully searched with the Adobe PDF search function.

To navigate to the WoEs, open the bookmarks panel and click on the heading or bookmark for the paper/report of interest (see screen-shot below). To return to your previous location, used the “back button” as shown.



Each major heading is followed by an enlarged copy of the relevant figure from the paper. This figure is followed by one or more figures that include a key to all the data points on the main figure. These a listed by number and study and response number is shown in a table on the right of the figure. To navigate to a specific study and response, click on the relevant cell in the table and this will take you to page on which that response is evaluated. To return to the previous view, click on the button shown in the above diagram.

Colony-level toxicity studies with TMX in honeybees

(*A figure is not included in this section*)

(Syngenta 2015)

Report: Syngenta. 2015. Thiamethoxam Technical – Honey Bee Brood and Colony Level Effects Following Thiamethoxam Intake via Treated Sucrose Solution in a Field Study in North Carolina. Greensboro, United States: Syngenta Ltd. (Unpublished Report). Report S14-02633. 468 p

The objective of the study in central North Carolina (NC, USA) was to evaluate consistently the effects of TMX exposure on honeybee colony condition that may impact long-term survival of honey bee colonies. A feeding study was conducted in the field whereby free-foraging colonies of honeybees (*Apis mellifera*) were exposed to multiple exposure concentrations of TMX in a sugar solution.

Responses 1-11: Quality of methods		Score
Experimental design and hypotheses	There were 6 treatment groups: five with TMX nominal exposure concentrations of 12.5 (T1), 25 (T2), 37.5 (T3), 50 (T4) or 100 ppb (w/w = mg/kg) (T5) and 1 control with untreated sucrose (UTC). These correspond to measured mean concentrations of 9.3, 24.1, 29.5, 39.7 and 73.8 µg/kg, respectively (Table 70) in the verification samples. Stability samples were prepared in sealed vials and stored in the hives for the period of exposure (Table 70); however, as these samples were not exposed directly to the environment of the hive, they were not used in characterizing toxicity. The TMX treatments comprised 12 replicate colonies per treatment, whereas the untreated control had 24 replicate colonies for a total of 84 hives + 12 monitoring hives for QA purposes. Fresh feeding solution volumes of 1000 – 1500 mL were placed inside hives using Boardman Feeders and renewed twice weekly over a 6-week exposure period (12 feeding events from 1 wk after CCA3 to CCA5); dosing started on July 8, 2014 and ended August 19, 2014. Supplemental feeding occurred in fall and for overwintering hives, as needed. Assessments were made to evaluate the overall colony performance at several times during and after the exposure period (41-d or 6 weeks), as well as in the fall and following spring. The initial two CCAs (CCA1 and CCA2) were initiated on 20 May 2014 to monitor the establishment of colonies from packages and to select the 84 hives needed for the study. CCAs continued for the study on 02 - 06 Jul 2014 (CCA3), 28 – 31 Jul 2014 (CCA4), 20 – 28 Aug 2014 (CCA5), 17 – 23 Sep 2014 (CCA6), 06 – 10 Oct 2014 (CCA7), 27 – 29 Oct 2014 (CCA8) and after overwintering on 31 Mar 2015 (CCA9) and 28 - 29 Apr 2015 (CCA10). The colony assessments generated data for colony Quality (number of adult bees, hive weights), presence of a healthy queen, colony development (pupae, larvae, eggs), and pollen & nectar stores; disease & infestations were assessed as well as overwintering success. The study occurred near Greensboro, NC in an area with mostly managed pasture and forest lands but there were small tracts of agriculture land with corn, soybean, and tobacco. The origin of the colonies was well described and acquired from commercial sources. The bees were installed in new hive boxes on May 3, 2014 and then ordered into 12 apiary groups based on brood Quality. 8 hives were established at each site (7 + 1 monitoring hives). The hives were moved to the field sites between June 27 and July 1, 2014 (p 24). At CCA3 which was the	**4**

	start of the TMX sugar solution dosing period, each colony consisted of one to two brood boxes with 10 frames in each box and 3689 to 22081 honeybees per colony (Tables 21-26) estimated according to Imdorf & Gerig[2], and Imdorf et al[3]. Manual and digital imaging methods were well described. Samples of hive matrices were collected from the treatment and control hives to monitor residues of the test material during the study. Handling methods and storage conditions of samples were well described (p. 29). The colonies were managed as typical for good apicultural practice in the region, including applying miticide treatments (Apiguard®), performing beekeeper checks for swarm control and providing supplemental food during periods of dearth as required to maintain colony vitality (with the exception that start of winter feeding was initiated later than recommended and probably impacted overwintering survival). Any applications of pest control treatments or supplemental feeding were made based on the assessments of control hives. Hive wts were digitally recorded continuously and verified manually 1 wk before the CCA3 and at all dates where digital balances failed. Stored bee bread and nectar were collected from uncapped cells and from capped cells with honey and bee bread on 3 occasions for residue analyses (Tables 68-69). Pollen was collected from pollen traps 8 times (p 21). Exposure concentrations were verified (Table 70) using 2 independent samples on 2 separate occasions and stability of the material evaluated & reported. Occurrence of *Varroa* mite in the colonies was assessed by sampling hive bees once before start of exposure (CCA3), once after exposure before overwintering (CCA5) and once after overwintering (CCA9). The number of *Nosema* spores per bee was determined once during the study after overwintering (CCA9) QA included: at least two days between feeding events; documenting the amount of dosing solution consumed for each hive; evaluating the stability of the TMX in sugar solution stored under ambient conditions in hives (Table 70); environmental conditions such as temperature (daily minimum/maximum), relative air humidity (daily minimum/maximum); rainfall; and historical (10 year minimum) average precipitation and minimum/maximum air temperature data from the nearest weather station that provides such data (Tables 4 to 14). Source of pollen was identified using paleonology methods. Statistical procedures were described (Subsection 3.8; p 32) and standardized methods (ISO Guidance Document 54) were applied to the data, and P values reported. Assumptions of models were tested and appropriate action taken when violated.	

[2] Imdorf, A and L. Gerig (1999): Lehrgang zur Erfassung der Volksstärke, Schweizerisches Zentrum für Bienenforschung. [Course in Determination of Colony Strength, Swiss Bee Research Center].

[3] Imdorf, A., Buehlmann, G.; Gerig, L.; Kilchmann, V. And Wille, H. (1987): Überprüfung der Schätzmethode zur Ermittlung der Brutfläche und der Anzahl Arbeiterinnen in freifliegenden Bienenvölkern, Apidologie 18 (2), 137 – 146. [A Verification of the Method for Estimation of Brood Areas and Number of Worker Bees in Free-Flying Bee Colonies].

Use of GLP and QA/QC.	The study was a GLP study with QA and QC documented; amendments to study plans, signatures, audits etc. Study plan was included and all deviations reported.	**4**
Exposure concentrations	Exposure concentrations were verified analytically (Subsection 3.5.5); stability verified (Table 70). Storage and shipping conditions documented (Tables 66 and 67). Sample analyses was GLP and QA statement included (Appendix 4). There were five TMX exposure concentrations that spanned the effect range and a control.	**4**
Transparency of data.	All data and summaries were clearly presented.	**4**
Number of samples and replication.	The replication was robust compared to most other field studies conducted with neonicotinoids. Five TMX exposure concentrations and 12 apiary groups; at each site, there were 7 hives + 1 monitoring hive for the TMX-treated sites and 24 hives per control treatment for a total of 96 hives. Repeated measures were taken and sample sizes ranged from 3-8.	**4**
Overall evaluation of methods		**4.00**
Score for expert judgment on quality of the study	**1**	**4.00**

Response 1. Effects on overwintering success of colonies exposed to multiple concentrations of TMX in a sugar solution.		**Score**
Statistical significance of responses	The late start of maintenance feeding after the dosing phase and before winter resulted in low bee populations going into winter, and when coupled with a very cold period in early spring, many colonies did not survive the over-wintering period. Therefore, overwintering data were reported but are not used for interpretation and conclusion related to over-wintering success between treatments. From the 12 sites with a combined 84 hives, 69 hives were considered dead by 28 Apr 2015 (end of study; Figure 9).	**0**
Concentration- or dose-response	There were no significant effects attributed to TMX and a concentration-response was not observed.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	19/24 control colonies died and there was no concentration exposure effect. The lack of overwintering success was attributed to other factors see above.	**0**
Mechanism and or mode of action of effect explained	It is reasonable considering the effects on control hives that bee husbandry and climate were directly linked to overwintering failure.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on colony Quality of exposure to multiple concentrations of TMX – number of honeybees		**Score**
Statistical significance of responses	The mean colony Quality was similar for all treatment groups except T5 (73.8 µg/kg) until start of over-wintering (Figure 1). Slight fluctuations in the mean number of honey bees per colony were considered normal, reflecting the weather conditions and seasonally changing food supply. The number of bees exposed to T5 (73.8 µg/kg) were significantly lower than that of the control in August, September, and October 2014 (1-sided Ancova; $p \leq 0.05$; pre-treatment adjusted) (p. 37). Digital imagery confirmed the reductions at 73.8 µg/kg at the end	**4**

	of August to September (Dunnett's test, one-sided, p ≤0.05; Table p 43 & Figure 8).	
Concentration- or dose-response	A concentration response was observed. The LOAEC was 73.8 µg/kg and the NOAEC was 39.7 µg/kg.	**3**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The small and unevenly distributed number of surviving colonies does not allow any scientifically-based conclusion about treatment-related overwintering success.	**0**
Mechanism and or mode of action of effect explained	No specific mechanism was suggested or investigated but TMX was clearly toxic at the highest exposure concentration.	**0**
Overall evaluation of relevance (computed)		**1.75**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on hive weight of exposure to multiple TMX concentrations in a sugar solution.		**Score**
Statistical significance of responses	All hive weights decreased after post-dosing supplementary feeding was terminated. The 9.3 µg/kg and 73.8 µg/kg hives exhibited slightly greater weight losses in August and September 2014, but rebounded to weights in October 2014 that were similar to the weights of hives of the other treatment groups. In general, no dose response trend was evident in hive weights. During the winter, the weights of all colonies followed a similar oscillating pattern.	**0**
Concentration- or dose-response	No dose response trend was evident in hive weights.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed but it is clearly toxicity.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on brood development resulting from exposure to multiple concentrations of TMX in sugar solution – brood nest size		**Score**
Statistical significance of responses	The development of the mean brood nest size until start of over-wintering was similar for all treatment groups except T3 (24.1 µg/kg) and T5 (73.8 µg/kg). Slight fluctuations in the brood nest size could be regarded as normal (Table p. 38). Brood nest size was significantly reduced by the highest concentration of 73.8 µg/kg on CCA-4, 5, and 6 (end of July to end of September) (1-sided Ancova, p ≤0.05; pre-treatment adjusted; Figures 1 and 2).	**4**
Concentration- or dose-response	Brood nest - the LOAEC was 73.8 µg/kg and the NOAEC was 39.7 µg/kg. There was a concentration-response.	**4**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	At the 738 µg/kg treatment level, multiple endpoints were significantly affected during of the study. Significant adverse effects for various endpoints were also observed at the 29.5 µg/kg and at 24.1 µg/kg treatment levels; however, these effects were transient and did not result in significant reduction in hive Quality (number of adults) over the course of the study unlike the 73.8 µg/kg treatment where hive Quality	**3**

	was significantly reduced at several CCAs. Therefore, the lowest observed adverse effect level (LOAEC) was determined to be 73.8 µg/kg and the no observed adverse effect level (NOAEC) was determined to be 39.7 µg/kg.	
Mechanism and or mode of action of effect explained	No mechanism and/or mode of action was proposed but it is clearly toxicity.	**0**
Overall evaluation of relevance (computed)		**2.75**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on brood development resulting from exposure to multiple concentrations of TMX in sugar solution - nest area with eggs		**Score**
Statistical significance of responses	For eggs – significant reductions occurred from end of August to end of September at 738 µg/kg with an inconsistent reduction at 9.3 µg/kg at the end of September (Table on p. 39, Figure 3).	**4**
Concentration- or dose-response	Egg cells - the LOAEC was 73.7 µg/kg and the NOAEC was 39.7 µg/kg. There was a concentration-response.	**4**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The lowest observed adverse effect level (LOAEC) was determined to be 73.8 µg/kg and the no observed adverse effect level (NOAEC) was determined to be 39.7 µg/kg because the adverse effect observed for the 9.3 µg/kg treatment occurred only once. At the last CCA before over-wintering (CCA8) colonies of all treatment groups had a similar proportion of egg and larval cells.	**3**
Mechanism and or mode of action of effect explained	No mechanism and/or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**2.75**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on brood development resulting from exposure to multiple concentrations of TMX in sugar solution - nest area with larvae		**Score**
Statistical significance of responses	The effect observed for larval cells was similar to that for egg development - significant reductions occurred from end of August to end of September at 73.8 µg/kg with an inconsistent reduction at 24.1 µg/kg at the end of October but only when the numbers were unadjusted (Table on p. 39; Figure 4).	**4**
Concentration- or dose-response	Larval cells - the LOAEC was 73.8 µg/kg and the NOAEC was 39.7 µg/kg. There was a concentration response.	**4**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The lowest observed adverse effect level (LOAEC) was determined to be 73.8 µg/kg and the no observed adverse effect level (NOAEC) was determined to be 39.7 µg/kg because the adverse effect observed for the 24.1 µg/kg treatment occurred only once. At the last CCA before over-wintering (CCA8), colonies of all treatment groups had a similar proportion of egg and larval cells.	**3**
Mechanism and or mode of action of effect explained	No mechanism and/or mode of action was proposed but it is clearly toxicity.	**0**
Overall evaluation of relevance (computed)		**2.75**
Overall evaluation of relevance (SEJ).		

Response 7. Effects on brood development resulting from exposure to multiple concentrations of TMX in sugar solution - nest area with pupae.	**Score**

Statistical significance of responses	For pupal cells – there were significant reductions from the end of July to the end of September at 73.8 µg/kg, from the end of July to the end of August 2014 (Ancova, one-sided, p ≤0.05, pre-treatment adjusted) at 39.7 µg/kg and at 24.1 µg/kg only once at the end of August 2014 (Table on p. 40; Figure 5). The latter exhibited a concentration-response relationship. At the last CCA before over-wintering (CCA8) colonies of all treatment groups had a similar proportion of pupae in cells	**4**
Concentration- or dose-response	Pupal cells – the LOAEC was 39.7 and the NOAEC 29.5 µg/kg. There was a concentration-response.	**4**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Because the cells with pupae were observed to be adversely affected in three treatments and the duration of the adverse effects persisted over time in a dose-dependent manner, the LOAEC was determined to be 39.7 µg/kg and the NOAEC was 29.5 µg/kg.	**3**
Mechanism and or mode of action of effect explained	No mechanism and/or mode of action was proposed but it is clearly toxicity.	**0**
Overall evaluation of relevance (computed)		**2.75**
Overall evaluation of relevance (SEJ).		

Response 8. Effects on food storage by honeybees resulting from exposure to multiple concentrations of TMX in sugar solution – cells filled with nectar/honey and pollen/bee bread combined.		**Score**
Statistical significance of responses	When all food stores were considered there were no significant differences in food stores by honeybees attributable to exposure to TMX (p. 41).	**0**
Concentration- or dose-response	There was no apparent exposure concentration-response relationship.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	There was no consistent pattern to the “transient” significant responses except for the highest exposure concentration of 73.7 µg/kg. That said, in the last assessment before the overwintering period, food storage by bees was similar and supplementary feeding post-exposure had started.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 9. Effects on food storage by honeybees resulting from exposure to multiple concentrations of TMX in sugar solution – cells filled with nectar/honey.		**Score**
Statistical significance of responses	When all food stores were considered there were no significant differences in food stores by honeybees attributable to exposure to TMX (p. 41); for cells filled with honey/nectar in hives, there were no significant adverse effects observed before overwintering (Table on p. 41; Figure 6).	**0**
Concentration- or dose-response	There was no apparent exposure concentration-response relationship.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant adverse response was observed, there was no relevance to apical endpoints.	**0**

Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on food storage by honeybees resulting from exposure to multiple concentrations of TMX in sugar solution – cells filled with pollen/bee bread.		**Score**
Statistical significance of responses	When all food stores were considered there were no significant differences in food stores by honeybees attributable to exposure to TMX (p. 41). For cells filled with pollen/bee bread, there were significant reductions at the end of July and August 2014 at 29.5 and 73.8 µg/kg and a single significant reduction at 39.7 µg/kg at the end of July 2014 (Table on p. 42; Figure 7). Despite the latter, the pollen stores of all colonies were similar before overwintering. At the 24.1 µg/kg treatment, pollen stores were significantly lower than the UTC but this effect was not observed at the next higher treatment of 39.7 µg/kg.	**4**
Concentration- or dose-response	There was no apparent exposure concentration-response relationship.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	There was no consistent pattern to the “transient” significant responses except for the highest exposure concentration of 73.7 µg/kg. That said, in the last assessment before the overwintering period, food storage by bees was similar and supplementary feeding post-exposure had started. There were two sequential significant responses at 24.1 µg/kg but none at any time at 73.8 and 39.7but there was no concentration response so the NOEC was set at 39.7 µg/kg.	**2**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**1.50**
Overall evaluation of relevance (SEJ).		

Response 11. Effects on parasites and pests of honeybees		**Score**
Statistical significance of responses	No correlation between test item treatment and *Varroa* infestation level was detected. After over-wintering, the *Varroa* infestation levels were similar across all treatments ranging from 0.3 mites per 100 bees (T3,) to 0.6 mites per 100 bees (T2) (Figure 12, Tables 45 to 50). The number of *Nosema* spores per bee ranged from 750,000 (T2) to 3,966,667 spores per bee (T3). There was also no correlation with exposure to TMX and *Nosema* infestation (Table 51).	**0**
Concentration- or dose-response	There was no apparent exposure concentration-response relationship.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant adverse response was observed, there was no relevance to the apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no significant adverse response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 12. Effects on food consumption by honeybees exposed to multiple concentrations of TMX		Score
Statistical significance of responses	Hive sugar solution consumption rates ranged from 6910 mL to 14,000 mL of the total 14,000 mL per hive during 6-week dosing phase. The sugar solution to most hives in all treatments was consumed completely. Total sugar solution consumption is summarized in Tables 15 to 20. Figure 13 indicates that the amount remaining in the last 3 weeks increased at 73.8 µg/kg.	**4**
Concentration- or dose-response	Reduced consumption by honeybees was observed consistently at the highest exposure concentration only.	**1**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The consumption among all treatments was generally similar to that of the control honeybees.	**0**
Mechanism and or mode of action of effect explained	Since no significant adverse response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**1.25**
Overall evaluation of relevance (SEJ).		

Narrative

The highest residue values of TMX in bee bread samples taken at the end of exposure were 10.02 µg/kg in T1, 17.04 µg/kg in T2, 24.01 µg/kg in T3, 34.96 µg/kg in T4 (and 43.0 µg/kg in T5. After over-wintering the highest residues of TMX in bee bread samples were < LOQ in T2, 2.5 µg/kg in T3 and 4.1 µg/kg in T4. No hives survived winter in the T4 and T5. Clothianidin was detected above the LOQ only in one T3 hive at CCA5 (1.4 µg/kg). The highest residue values of TMX in nectar / honey samples taken at CCA5 were 17.7 µg/kg in T1, 27.6 µg/kg in T2, 28.1 µg/kg in T3, 61.8 µg/kg T4 and 102 µg/kg in T5. After over-wintering the highest residues of TMX in nectar / honey samples were 2.746 µg/kg in theT2, 5.1 µg/kg in the T3 and 21.9 µg/kg in T4.

In conclusion, at the 73.8 µg/kg treatment level, multiple endpoints were significantly affected at transient times during of the study. Significant effects in various endpoints were also observed at the 39.7 µg/kg and at 24.1 treatment levels; however, these effects were also transient and did not result in significant reduction in hive Quality (number of adults) over the course of the study unlike the 73.7 µg/kg treatment where hive Quality was significantly reduced at several CCAs. Therefore, the lowest observed adverse effect level (LOAEC) was determined to be 73.8 µg/kg and the no observed adverse effect level (NOAEC) was determined to be 39.7 µg/kg. There were no indications that exposure to TMX resulted in higher susceptibility of colonies to *Varroa* or Nosema infestation.

Pollen samples were collected eight times during the study for pollen source identification. The main plant species found over the course of the season were *Parthenocissus* sp. (Vitaceae), Zea mays (Poaceae), *Plantago* sp. (Plantaginaceae), *Chenopodium* sp. (Chenopodiaceae), *Lagerstroemia* sp. (Lythraceae), *Taraxacum* sp. (Asteraceae), *Helianthus* sp. (Asteraceae), *Liquidambar* sp. (Hamamelidaceae), *Nicotiana* sp. (Solanaceae), *Amaranth* sp. (Amaranthaceae), *Fagopyrum* sp. (Polygonaceae), *Rhus/Sumach* sp. (Anacardiaceae), *Glycine* sp. (Fabaceae), *Ambrosia* sp. (Asteraceae), *Trifolium* sp. (Fabaceae), *Xanthium* sp. (Asteraceae), *Tradescantia* sp. (Commelinaceae) and *Aster* sp. (Asteraceae). Most the pollen originated from local sources, bees clearly favored five types: *Chenopodium, Plantago, Rhus, Ambrosia, Helianthus* and Asteraceae-type. Secondarily, they foraged on plants such as *Parthenocissus* sp., *Zea mays* and *Lagerstroemia.*

Expert Judgement		
QA	Yes	June 2, 2016
SEJ	Yes	June 5, 2016

(Syngenta 2010a)
Report: Syngenta. 2010. Thiamethoxam (A9700B, A9584C) - A Semi-Field Study with Dust from A9700B treated Maize Seeds and A9584C to Evaluate Effects on the Honeybee *Apis mellifera* L. (Hymenoptera, Apidae) in *Phacelia tanacetifolia*. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10908 - A9700B, A9584C. 119 p

In 2009, a semi-field study using tunnels (OEPP/EPPO Guideline No. 170 (3))[4] was conducted in northern Germany near Eschede (Celle) to assess the effects of TMX on honey bees (*Apis mellifera* L.) applied as treated dust and as spray treatments of *Phacelia tanacetifolia*.

Responses 1-10: Quality of methods		**Score**
Experimental design and hypotheses	There were 5 treatment groups: three treatments applied during honeybee flight and the application rates (ARs) were 13.81 (T1) and 69.06 (T2) g TMX-dust/ha and 20.0 (T3) g (Actara - TMX) product/ha equal to 1.0, 5.0, and 5.0 g TMX/ha, respectively (measured). One treatment served as the experimental control (C) and was untreated and the fifth treatment (R) was a reference substance (dimethoate- 1L product/ha (400 g a.s./ha)); spray volume was 300 L/ha. The origin of the TMX-treated dust was from TMX-treated maize seed (7.24% w/w). The foliar application of TMX was as a flowable concentrate for seed treatment (FS 350) (verified analytically 342 g/L). Fungicide application of fludioxonyl/metalaxyl-M FS (025/010) (verified concentrations 24.6 and 9.94 g/L) were used. Actara was a formulation of TMX 25 WG (verified 25.2%). Purities and compositions were provided by the sponsor. Homogeneity of spray solution and stability was assumed (consistently weakness). ARs are provided in Section 3.3. Calibrated portable boom sprayer was used with fresh solutions to apply the treatments (see 3.4.4). For dust treatments (T1 and T2), the treated dust was mixed with a carrier (Schmelzflocken). For application, the crop area was divided into 20 sub-areas of 1.5 m^2 each and a defined amount of the mixture per sub-area was distributed by hand by sprinkling to distribute the dust. Products were applied on July 7, 2009. During application, the honeybee colonies were covered with plastic to prevent direct contamination. The volume applied was determined by subtraction and details provided in Tables 3-7. Certificate of seed analyses and product and material purity confirmation were provided (Appendix 1). Source of honeybees was not identified (*potential weakness*). Healthy hives with four combs each of which 2 had eggs, larvae and capped cells; one comb for honey and pollen; bees were free of disease (*Varroa* mites and *Nosema*) and were added to each tunnel on July 3, 2009, 4 d before the TMX was applied to the crop within each tunnel. Hives were equipped with dead bee traps (DBTs). There was only one field sown on May 7, 2009 with *P. tanacetifolia;* multiple tunnels (3 for each treatment; 12 in total) were established at full flowering. The area of a tunnel (11 x 5 x 3.5 m) was 55 m^2 with ~30 m^2 covered by the crop. Linen sheets (10 m^2) were placed in the tunnels at 3 locations (Figures 1-3). One honeybee hive was placed into each tunnel 4 days before the applications. For the control, T1, and T2 treatments there were 3 replicate tunnels per treatment; T3 (Actara) had 2 and the reference	**3**

[4] OEPP/EPPO (2001): Guideline for the efficacy evaluation of plant protection products – Side effects on honeybees. OEPP/EPPO, PP 1/170 (3) update 2000, 19 - 23.

	treatment had one tunnel. Meteorological data were collected and reported (Tables 8-9). Mortality, behaviour and foraging activity of honeybees were assessed daily over seven days during the time of exposure in the tunnels and more frequently the day of application (e.g., before application and 1, 2, 4, 6 h after application). Furthermore, the mortality in dead bee traps only was assessed until DAA+21; field mortality assessments were conducted using linen sheets. The condition of the colonies and the development of the bee brood were assessed once before application and four times after application (DAA+7 to DAA+27; Tables 20-24); Assessments followed cited methods. Pollen samples were collected from combs for residue analyses on two occasions (DAA+7 – July 14, 2009; and DAA+27 – August 3, 2009) post application (Table 30) and frozen during shipment and storage (Appendix 3 contains analytical results, LOD ad LOQs). Methods were described, recoveries included and QA measures provided. Statistical procedures were applied to the data (see subsection 3.7).	
Use of GLP and QA/QC.	GLP study; QA statement; audits. No study plan but amendments were included. Analytical chemistry was GLP and assessment methods followed standard practices. Residues measured in pollen	**4**
Exposure concentrations	There were two exposure concentrations 1.0, 5.0, TMX in dust with Schmelzflocken and 5.0 g TMX (Actara)/ha for T1, T2 and T3 and an experimental control. There were either 2 or 3 replicate tunnels each sprayed independently and each had one hive.	**4**
Transparency of data.	Raw and summary data were provided.	**4**
Number of samples and replication.	One field with flowering crop. There were 12 tunnels set up on the field and each tunnel was sprayed independently. There was one hive per tunnel and either 2 or 3 tunnels per treatment.	**2**
Overall evaluation of methods		**3.40**
Score for expert judgment on quality of the study-	**1.0**	**3.40**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	Pre-application mortality was similar among treatments. Significant effects on mortality were seen at 1 and 5 g TMX/ha applied in dust (T1 and T2) and in T3 (5 g TMX (Axtara) /ha) applied as spray product A9584C relative to that for the control treatment (Dunnett's test, 1-sided, p ≤0.05). At DAA+1 the mortality was 91.7, 639.3 and 68.0 dead bees in T1, T2 and T3 respectively compared with 5.7 dead bees in the control. The mean post-application mortality (DAA0aa to +21) was shown in Figure 4 to be significant in all three test item treatment groups, 21.5, 66.8, 32.7 dead bees in T1, T2 and T3, respectively, compared to 6.5 dead bees in the control, so a NOEC for mortality could not be derived for any treatment (Subsection 4.1; Tables 10-14).	**4**
Concentration- or dose-response	The lowest application rate of 1 g a.s./ha significantly adversely affected survival of honeybees. Mortality appeared to be exposure dependent in that mortality was greater at the higher concentration in dust. Foliar application significantly increased mortality relative to the controls but a dose-response could not be discerned because there was only one level.	**1**

Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Honeybees exposed to TMX in dust and survival of foragers were adversely affected.	**4**
Mechanism and or mode of action of effect explained	No explanation was suggested but the obvious explanation is the direct application of an insecticide.	**4**
Overall evaluation of relevance (computed)		**3.25**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	Flight intensity as reflected by the number of forager bees/m^2 was similar among treatments prior to application of the treatments (see subsection 4.2; Figure 5). Significant reductions in flight activity were observed at T2 (5 g TMX/ha in dust) and T3 (5 g TMX (as Axtara)/ha in A9584C) on days 5 and 6 post application but overall there was no significant different of the mean flight intensity. An NOEC of 1 g TMX/ha in dust (T1) was derived for flight intensity (Tables 15-19). An unbounded LOAEC was derived (5 g TMX/ha) for flight intensity in the A9584C spray treatment.	**4**
Concentration- or dose-response	There did not appear to be a significant concentration-response relationship.	**1**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Significant effects were observed that could be interpreted as either adverse (i.e., a reduction in the number of foraging flights undertaken from the colonies) or beneficial (i.e., behavioural avoidance) which reduces the number of visits to the treated plots and ultimately exposure to TMX. Regardless, these effects were not reflected in the hive endpoints (see below).	**3**
Mechanism and or mode of action of effect explained	No mechanisms were provided or proposed but insecticidal activity is a likely cause.	**2**
Overall evaluation of relevance (computed)		**2.50**
Overall evaluation of relevance (SEJ). The significant adverse effect occurred on Day 5 and Day 6 but did not persist over the duration of the study and no lasting adverse effects were observed for the development of the colonies. A lower score was assigned because the effect was observed on one day only.		**1**

Response 3. Effects on honeybee behaviour		**Score**
Statistical significance of responses	TMX-related effects on behaviour were observed on the day of application in all test item treatment groups – T1 (1 g TMX/ha in dust), T2 (5 g TMX/ha in dust) and T3 (5 g TMX/ha applied as spray product A9584C) and in T1 and T2 on the following 2 days (Tables 25-29). Intoxication behavior was observed after treatment and persisted for a few days. A NOEC could therefore not be derived.	**4**
Concentration- or dose-response	There was no obvious concentration response relationship.	**1**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Intoxication symptoms post application persisted and might have contributed to the decrease in brood nest size and increased mortality observed within the 7-d exposure period.	**2**
Mechanism and or mode of action of effect explained	No mechanism was investigated or proposed but insecticidal activity is a likely cause.	**2**

Overall evaluation of relevance (computed)	**2.25**
Overall evaluation of relevance (SEJ).	

Response 4-5. Effects on colony Quality - # adult bees & brood nest size		**Score**
Statistical significance of responses	The colony Qualitys in terms of number of bees were similar among treatments before application of the chemicals and ranged between 2363 and 3207 bees (Figure 7). The significant decrease in number of bees at the end of the 7-d exposure period occurred in all TMX treatments regardless of the exposure concentration (Figure 7). The mean Quality of the colonies increased in the control (Table 20) and in T2 (Table 22) until the last brood assessment by 6.5 % and 27.0 %, respectively, and declined by 8.3 %, 5.9 % and 8.8 % in T1 (Table 21), T3 (Table 23) and R (Table 24), respectively, until the last brood assessment on DAA+27. Between the assessments on DAA-5 and DAA+7 the number of bees decreased statistically significantly in T1, T2 and T3 in comparison to the control (Dunnett's test, 1-sided, $p \leq 0.05$), and in T2 also on DAA+14 (Figure 7). Brood nest size was similar among treatments (Figure 6). The decrease in brood nest size was uniform for all treatments including the control treatment which the authors state is typical for tunnel experiments and a reflection of unfavourable foraging conditions inside the tunnels.	**4**
Concentration- or dose-response	There was no obvious concentration response relationship.	**1**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The decrease in colony Quality as reflected by the decrease in the adult bee population of exposed hives ultimately could affect hive productivity.	**3**
Mechanism and or mode of action of effect explained	Initial decrease in Quality was likely due to significant mortality in the early part of the exposures. The decrease in brood nest size was uniform for all treatments including the control treatment which is typical for tunnel experiments and a reflection of unfavourable foraging conditions inside the tunnels.	**2**
Overall evaluation of relevance (computed)		**2.50**
Overall evaluation of relevance (SEJ).		

Response 6-8. Effects on colony Quality -brood development		**Score**
Statistical significance of responses	No statistically significant effects on the proportion of the different brood stages and the total proportion of brood were observed at any of the assessment dates (Figures 8-11). No TMX related effects were observed on the brood development of the bees compared with the control. Thus, a NOEC for brood development of 5 g TMX/ha was derived for both dust and spray treatments.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not observed but an unbounded NOAEC was calculated	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed	**0**

Overall evaluation of relevance (computed)	**0.00**
Overall evaluation of relevance (SEJ).	

Response 9-10. Effects on colony Quality – food stores (nectar & pollen)		**Score**
Statistical significance of responses	There was a statistically significant decrease in nectar/food resources in T1 (1 g TMX/ha in dust) at the 2nd brood assessment at DAA+7 (Figure 9) compared to the control (Figure 8). A NOAEC for food resources for the dust treatment could not be derived but an unbounded LOAEC of 1 g/ha was derived. For the spray product A9584C, a NOAEC of 5 g TMX/ha was derived for food resources.	**4**
Concentration- or dose-response	No concentration response was observed, but an unbounded LOAEC and an unbounded NOAEC were derived for TMX and A9584C, respectively	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The depletion of food stores in all hives was attributed to an enclosure effect; however, there was a significant effect attributed to TMX at 1 g a.s./ha. A similar result was not observed at the higher treatment of 5 g a.s./ha.	**2**
Mechanism and or mode of action of effect explained	No mechanism was suggested or investigated.	**0**
Overall evaluation of relevance (computed)		**1.50**
Overall evaluation of relevance (SEJ). Food (pollen, honey, and nectar) from foraging bees is also adversely affected by confining the bees in tunnels.		**0**

Narrative

There were signs of honeybee intoxication within the 7-d exposure period at both exposures and significant effects on mortality and foraging intensity at 1 and 5 g TMX/ha (assessed daily from d-4 to d+21). No adverse effects on bee brood development were attributed to the exposure of the hives to the test item treated crop. A NOAER for behavior and mortality could not be determined because the effect range was unbounded. This level of toxicity is unexpected; however, it might be related to increased bioavailability of TMX from dust because of the carrier used to achieve a uniform distribution of dust on the plants. The test item was TMX-treated maize dust, screened to a particle size <500 µm. The treated dust was mixed with a ground and screened (particle size <550 µm) "Schmelzflocken" carrier to facilitate a homogenous distribution of the dust over the crop. The ratio of TMX to carrier was 1:500 and 1:100 for the two rates, respectively. Schmelzflocken "are processed from ground oat cores into tender melting flakes" and it is used as baby food[5]. It is possible that this made the mixture with the TMX dust attractive to the honeybees and it was gathered and consumed by honeybees as if it were pollen, resulting in the increase in mortality. In addition, the lowest rate of application was about 10-fold greater than those measured in deposition studies downwind of seeding of maize using a dust-deflector[6] where maximum values for deposition of TMX ranged from 0.03 to 0.11 g TMX/ha or the values measured in a very large study in Germany on deposition of dust during sowing of OSR[7] where the 90th centiles of deposition ranged from 0.0027 to 0.0052 g

[5] http://www.germandeli.com/Koelln-Schmelzflocken-250g-Oat-Flakes-8-8oz

[6] Syngenta. 2010. Evaluation of deposition of seed treatment particles abraded from "PRODUCT" dressed maize seeds emitted during sowing, in adjacent oilseed rape and bare soil areas Final Report Amendment No. 1. Frankfurt am Main, Germany: Syngenta Ltd. (Unpublished Report). No. A9700B_10906. 69 p.

[7] Syngenta. 2012. Thiamethoxam and CGA322704 - A9807C - Monitoring of the Deposition of Thiamethoxam and CGA322704 Dust Emitted During Sowing of Oil-Seed Rape Dressed with Cruiser

TMX/ha (QWoE for these studies below). Not having data on the attractiveness of this Schmelzflocken to honeybees, a tentative and conservative NOAER was derived from the lowest rate applied with an uncertainty factor of 10. This gave a NOAER was 0.1 g TMX/ha.

No residues of either TMX or clothianidin were found in any of the control samples or in the samples of the reference item treatment. No residues of clothianidin were found in any of the TMX treatment samples or reference item samples with one exception. On d 7 post application, a concentration of 0.003 mg/kg was measured in the pollen samples collected from T3. Residues of TMX ranging from <0.001 (T1) to 0.016 (T2) mg/kg were found in samples of pollen collected on DAA+7. On DAA+27 post-application, residues of TMX in pollen ranged from 0.012 to 0.028 mg/kg were detected in the TMX treatment groups.

Expert Judgement		
QA	Yes	June 2, 2016
SEJ	Yes	June 2, 2016

OSR (Germany, 2008). Maintal, Germany: Syngenta Ltd. (Unpublished Report). No. A9807C_10980 - A9807C. 58 p.

Risks to honeybees from exposures resulting from uptake and translocation of TMX from seed dressings

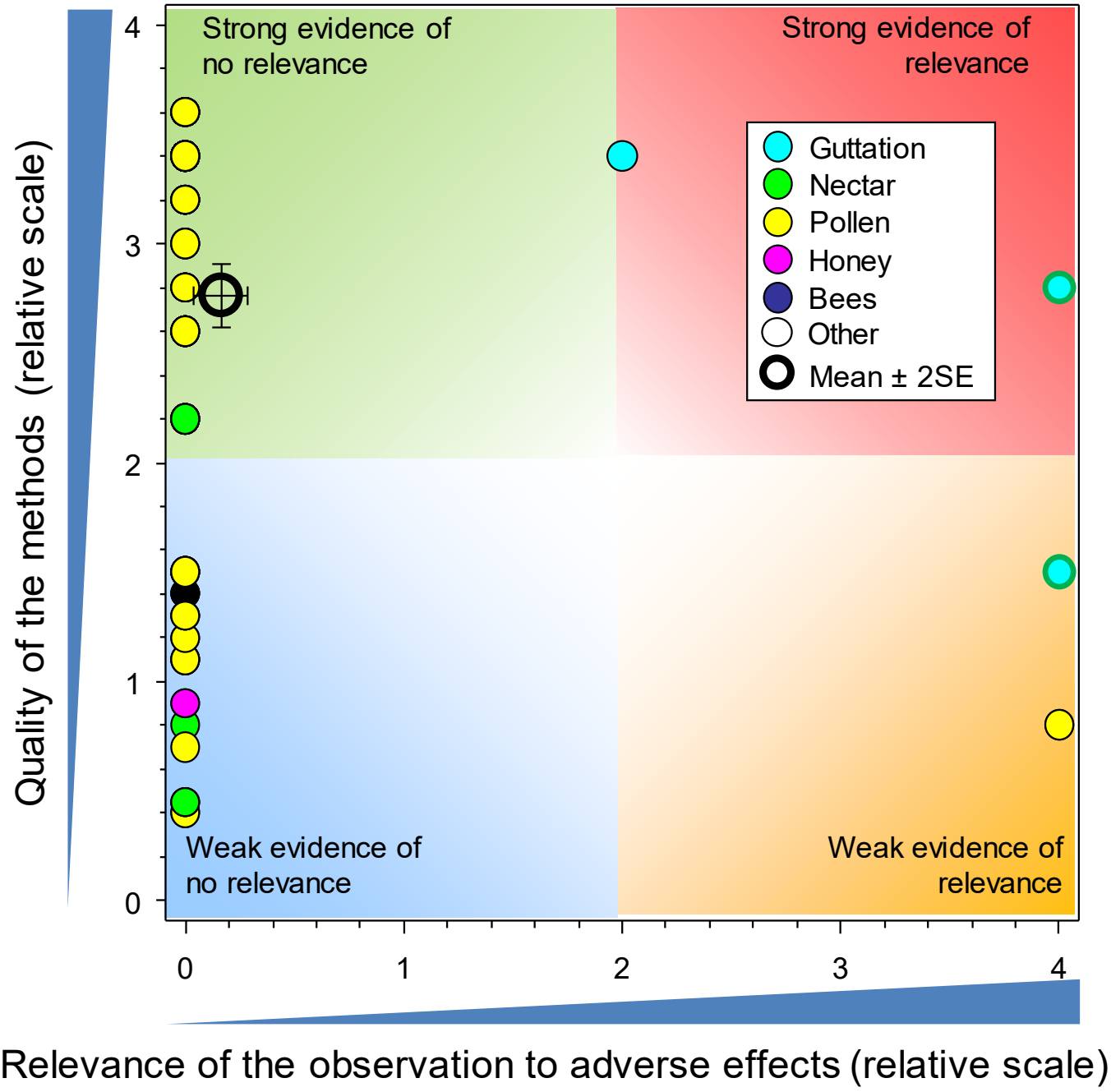
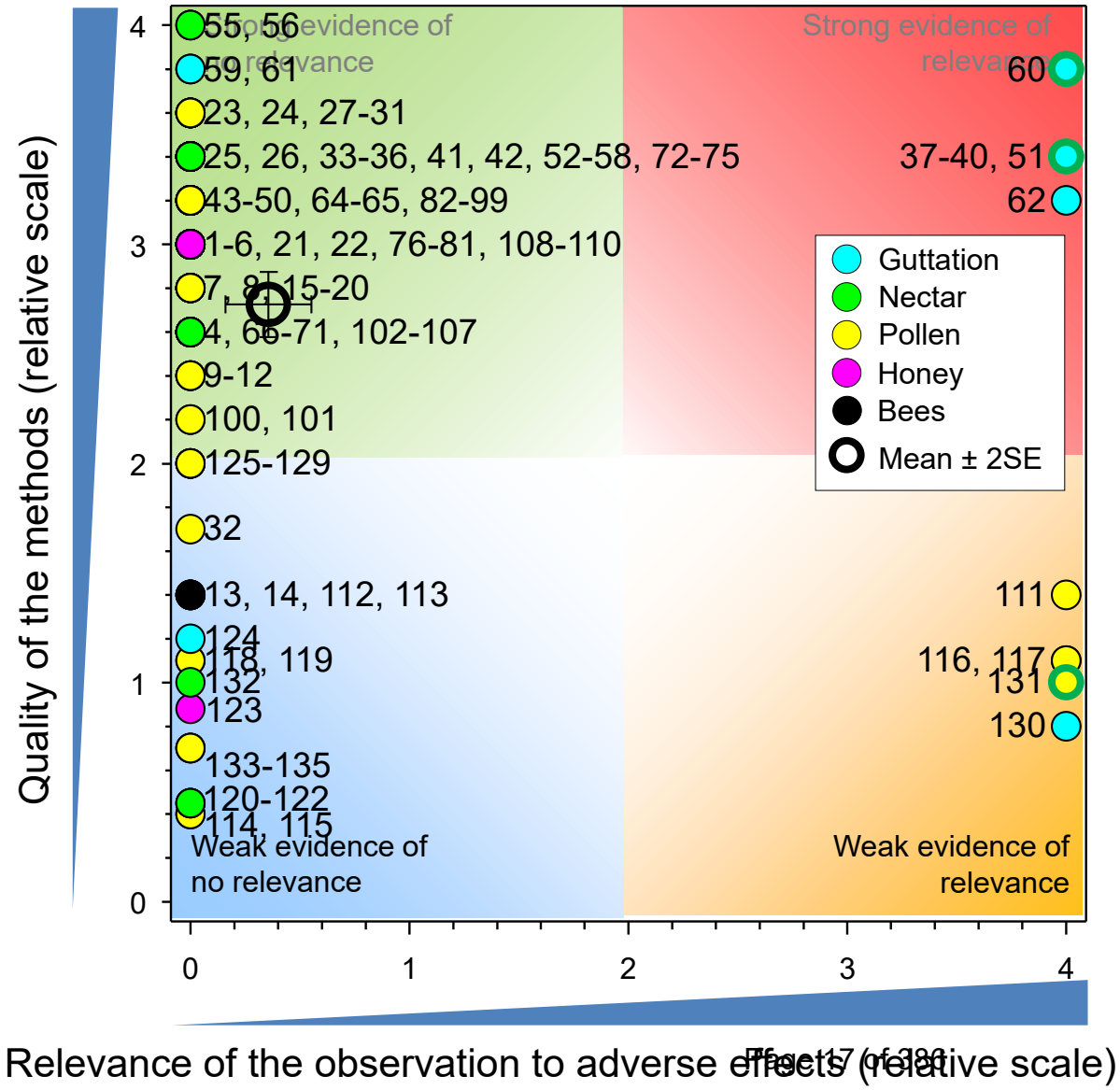


Figure 2. Quality and relevance of exposure values from controlled field studies with TMX treated seeds. Symbols may obscure others, see SI for all responses, n = 158. There were no points obscured by the legend. Points with a heavy green border did not demonstrate adverse effects in field studies.

Hazards of exposures of bees to CTD via seed treatments (SI)



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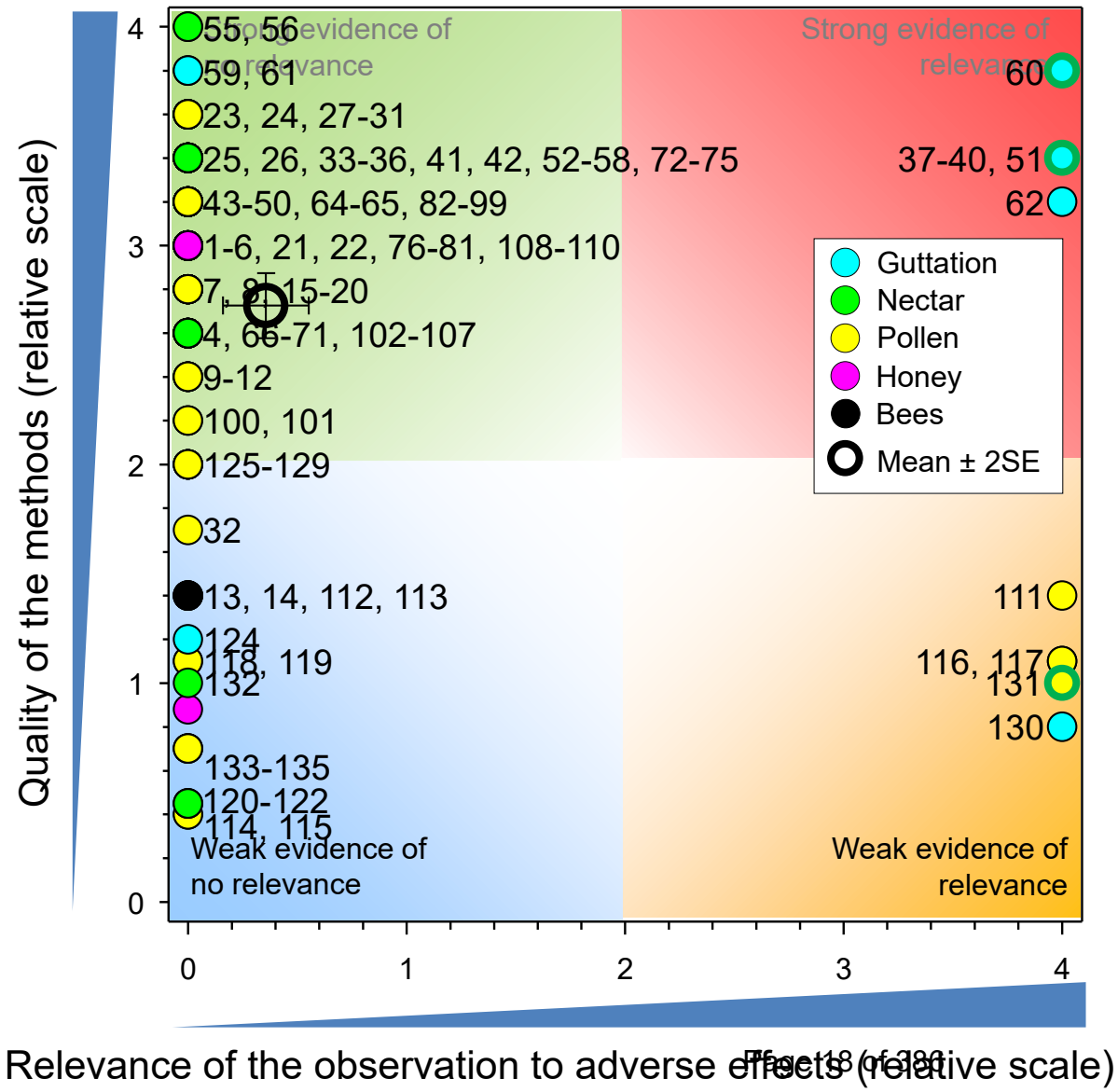
21 = (Bayer AG Crop Protection 2002c) Resp 1
22 = (Bayer AG Crop Protection 2002c) Resp 2
23 = (Bayer CropScience AG 2005a) Resp 1
24 = (Bayer CropScience AG 2005a) Resp 2

Hazards of exposures of bees to CTD via seed treatments (SI)



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29 = (Bayer CropScience AG 2007a) Resp 3
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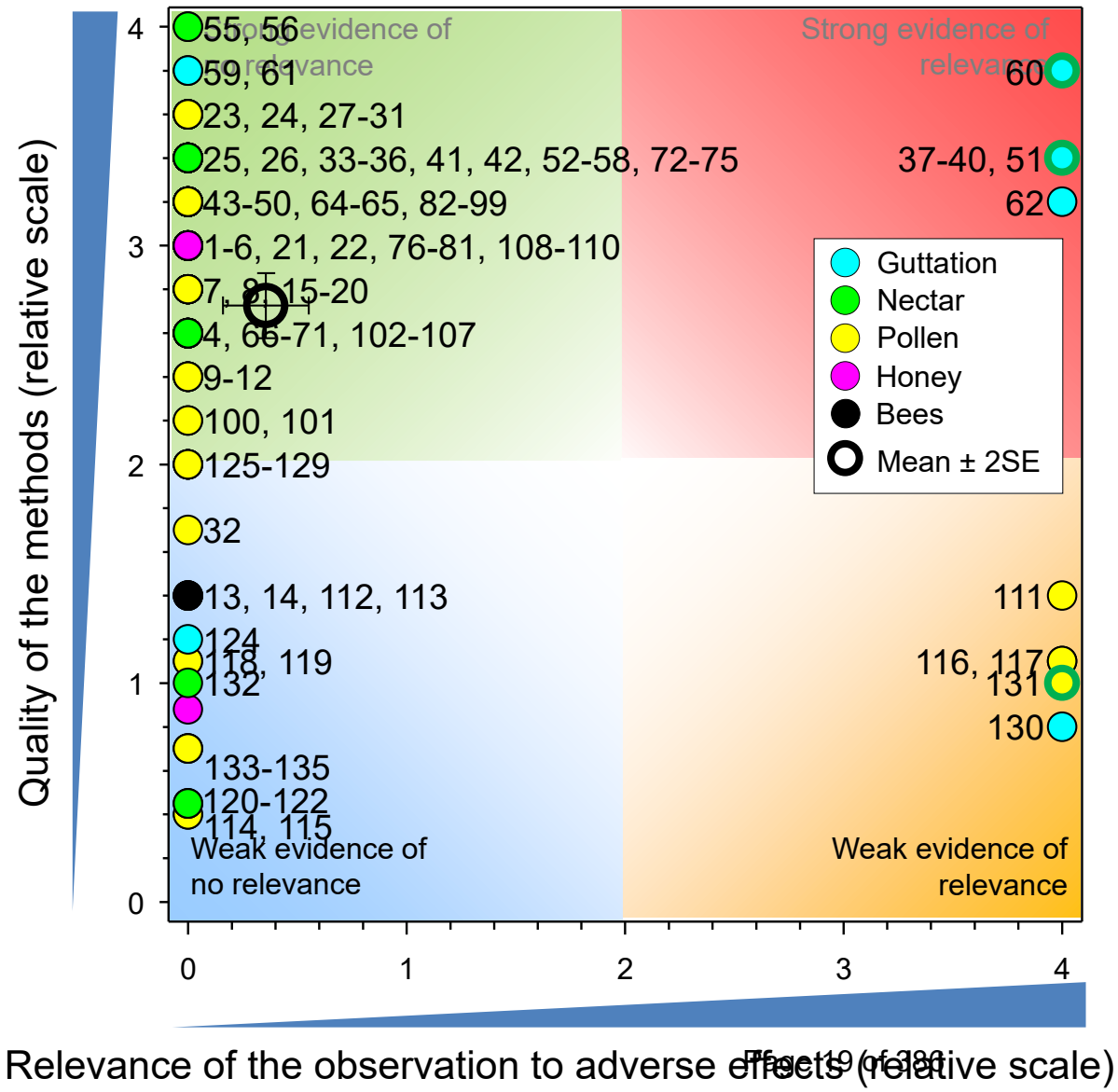
Hazards of exposures of bees to CTD via seed treatments (SI)



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54 = (Bayer CropScience 2012) Resp 4
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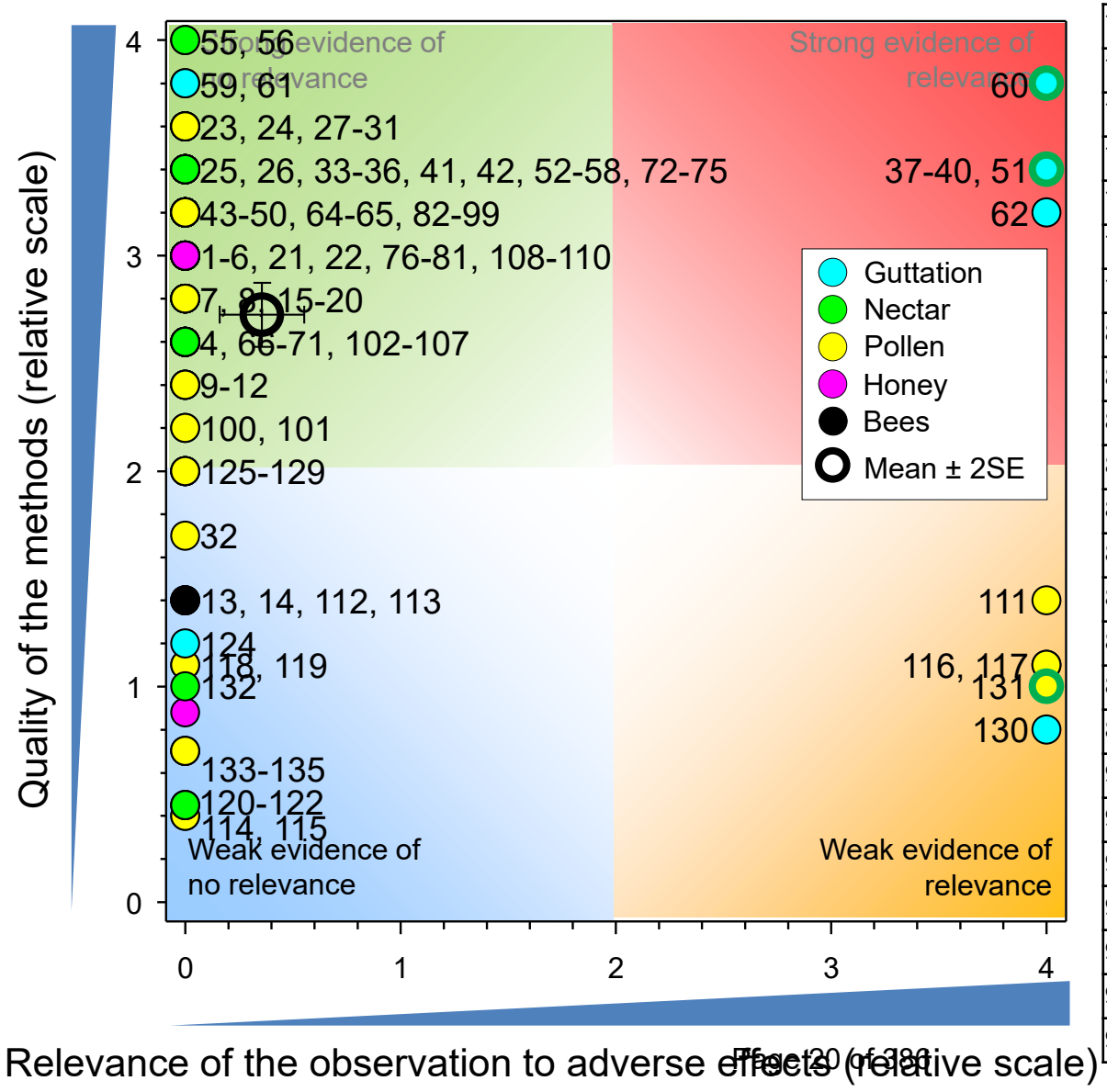
Hazards of exposures of bees to CTD via seed treatments (SI)



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94 = (Bayer CropScience 2015b) Resp 3
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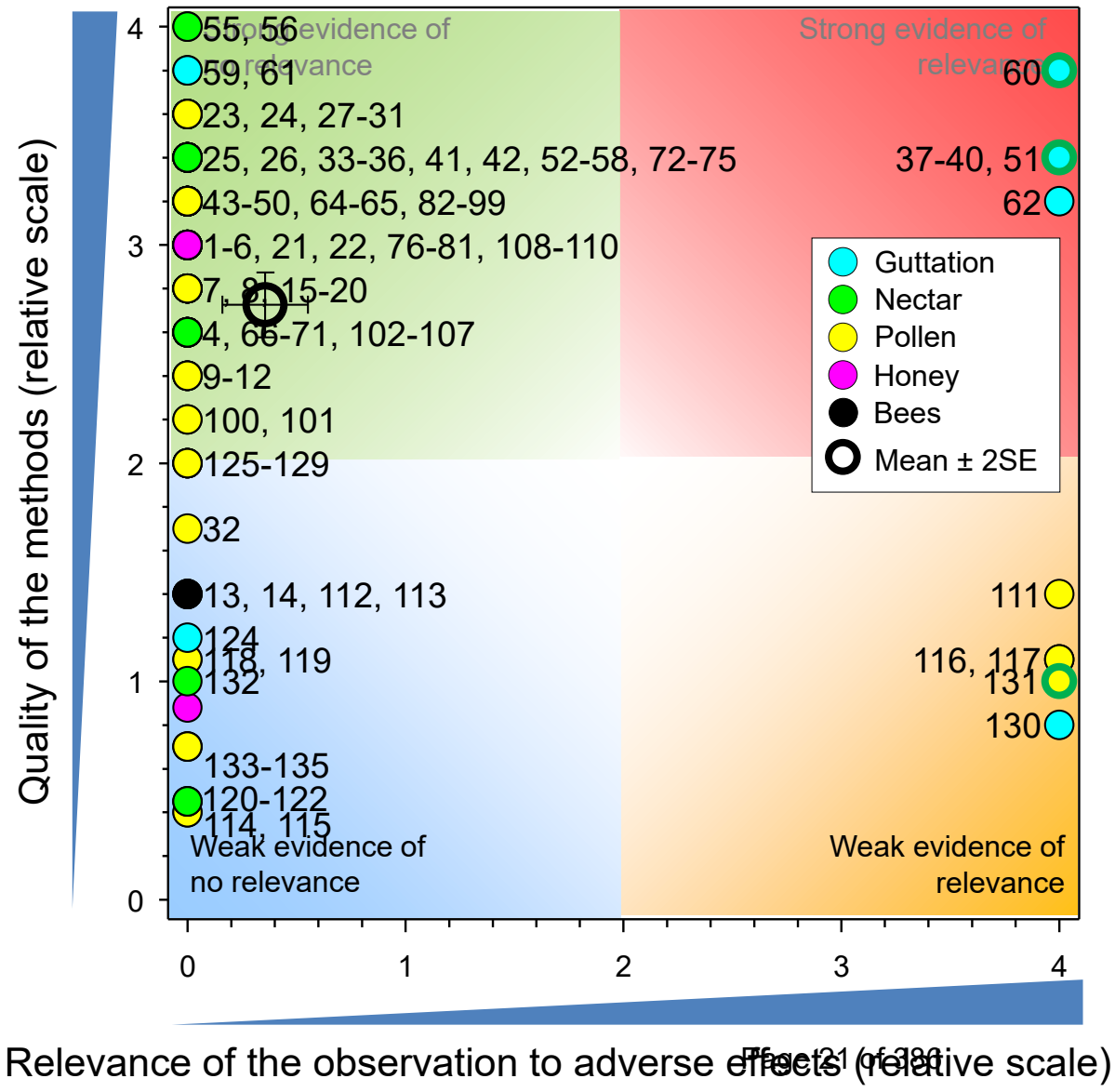
Hazards of exposures of bees to CTD via seed treatments (SI)



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102 = (Botias et al. 2015) Resp 1
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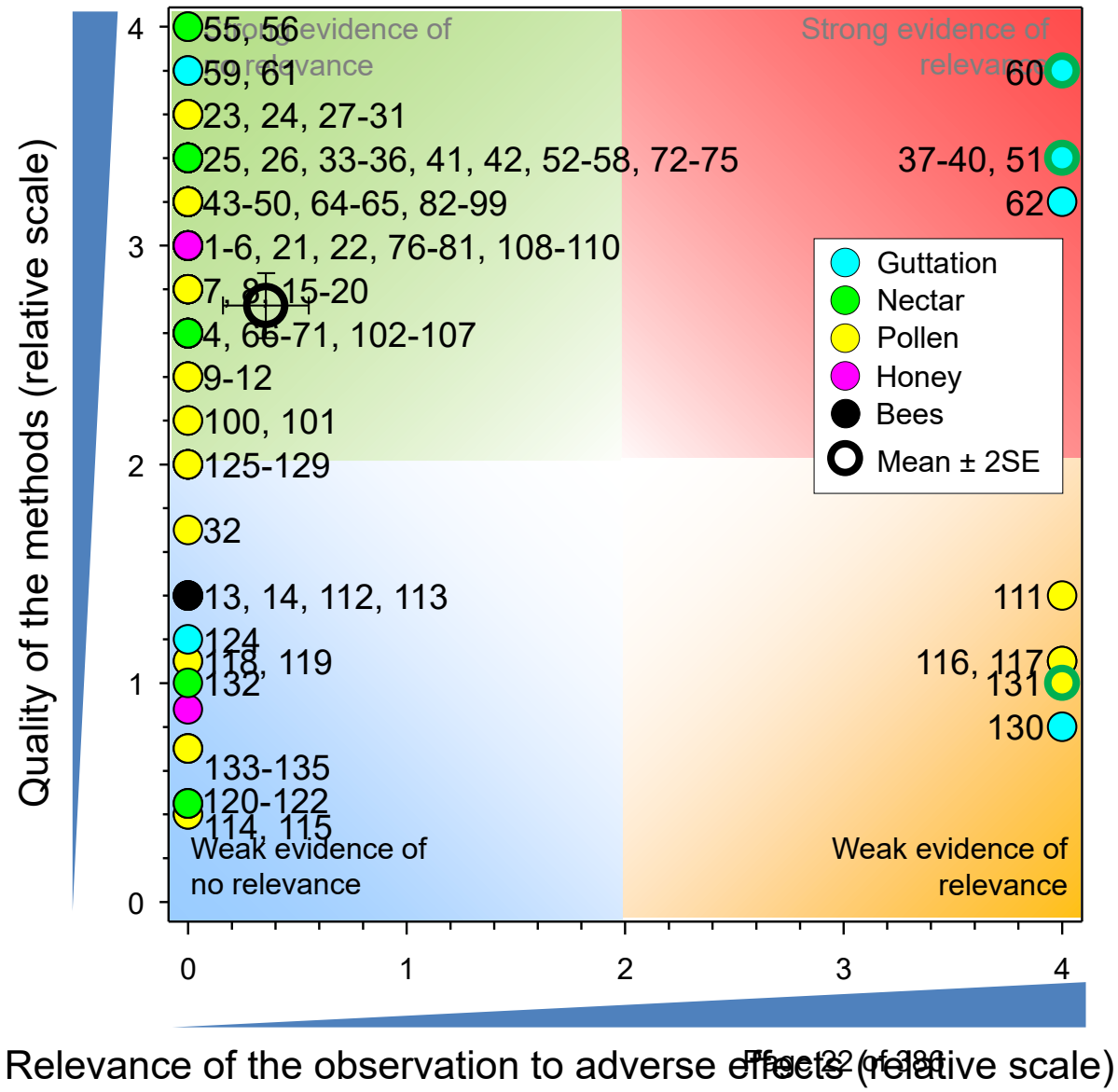
120 = (Krupke et al. 2012) Resp 7

Hazards of exposures of bees to CTD via seed treatments (SI)



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125 = (Pohorecka et al. 2012) Resp 1
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132 = (Rundlöf et al. 2015) Resp 2
133 = (Stewart et al. 2014) Resp 1
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135 = (Stewart et al. 2014) Resp 3

(Bargańska et al. 2013)
Paper: Bargańska Ż, Ślebioda M, Namieśnik J. 2013. Pesticide residues levels in honey from apiaries located of Northern Poland. *Food Control* 31:196-201.

This paper reported the concentrations of 30 pesticide residues found in honey samples collected in a northern region of Poland (Pomerania) in the year 2010. Only the data for TMX are assessed here.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	Forty-five honey samples of different origins were obtained from beekeepers of Pomerania (Poland) in the summer of 2010. The samples were supplied to the laboratory by the Regional Beekeepers Association in Gdansk and were packaged in glass containers. Information for collection of the samples and procedures to avoid contamination were not reported (weakness). All samples were kept at -10°C until analysis (less than the appropriate temperature of -20±4°C). No controls (field blanks), field, travel, and storage spikes were reported (**major weakness**). Samples of honey were homogenized and ca. 1 g was weighed into and extracted with 10 mL of acetonitrile,10 mL water and 50 µL of internal standard solution (triphenyl phosphate). Isotopically labelled internal standards for TMX were not used (weakness). The method of extraction and analysis was an adaptation of QuEChERS and was well described. Standards were obtained from a commercial source but purity was not reported. Concentrations of metabolites were not measured. Analysis was by LC/MS/MS. The analytical method was validated using a standardized method[8]. For TMX the LOD was 1.14 µg/kg, the LOQ was 3.42 µg/kg and recovery ranged from 84.9 to 85.5% (Author Table 2). Statistical analysis was not conducted but, curiously, the maximum values were reported with "expanded uncertainty", the calculation of which was not reported.	**2**
Use of GLP and QA/QC	This was not a GLP study. There was no QA and minimal QC.	**2**
Transparency of data	Raw data were not provided. Mean values were reported in a Table (3), only maximum and minimum values and frequency of detection were provided.	**2**
Number of samples and replication	There was no replication but independent 45 sites were sampled.	**3**

[8] SANCO/2007/3131. (2007). Method validation and quality control procedures for pesticide residues analysis in food and feed. < http://ec.europa.eu/food/plant/protection/resources/qualcontrol_en.pdf >.

Response 1: Quality of methods			Score
Duration of study sufficient to observe trends	The duration of sampling was not reported but was assumed to be appropriate for the design of the study.		**3**
Overall evaluation of methods	Computed mean of above		**2.40**
Score for expert judgment on Quality of the study. Lack of controls field, travel, and storage spikes and the storage temperature of >-18C		**0.5**	**1.20**

Relevance.

Hazard quotients for exposures to TMX in honey bees exposed via honey hives in Poland (data from Table 3).

Source	Matrix	Conc. TMX µg/kg	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg of food or water/d
Hives from Poland	Honey (max)	20.2	5.9	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in honey collected from hives in Poland resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 8, 2016
SEJ	Yes	May 29, 2016

(Botias et al. 2015)
Paper: Botias C, David A, Horwood J, Abdul-Sada A, Nicholls E, Hill E, Goulson D. 2015. Neonicotinoid residues in wildflowers, a potential route of chronic exposure for bees. Environmental Science & Technology 49:12731-12740

This study reported concentrations of neonicotinoids in soil, pollen, and nectar sampled from fields planted with winter oilseed rape (wOSR) in spring 2013 and soil, and nectar and pollen from wildflowers in the field margins from fields planted with wOSR and winter wheat (wW). Pollen collected from forager honeybees was also sampled. Analytes were CTD, thiamethoxam (TMX), imidacloprid (IMI) and thiacloprid. Only the results for TMX are included in this WoE.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	This study was conducted at five farms in East Sussex, UK in 2013. Seven fields of winter-OSR (sown late August 2012) and five fields of WW (sown late September 2012) were selected at random (methods not reported) from five farms in East Sussex, South-East England, UK. The selected fields had varying cropping history and pesticide use (data provided in Tables S1a-S1g) but followed normal farming practices in the region. The seeds of wOSR were all treated with Cruiser® seed dressing in 2012 (280 g/L TMX, 8 g/L fludioxonil, and 32.2 g/L metalaxyl-M). The wW seeds were treated with Redigo Deter® (50 g/L prothioconazole and 250 g/L CTD). The seeds used in these fields were not analyzed, although "representative" seeds used in the region were (*potential weakness*). The areas of the fields and the climatic conditions were not reported (*potential weakness*). Soil samples were taken in the fields and the margins and the presence of residues of CTD, TMX, and IMI were confirmed by analysis (data not discussed in this WoE). To obtain pollen samples, flowers of oilseed rape (≈1,000 flowers) were gathered and stored on ice in coolers in the field and then frozen immediately at -80°C until further handling. Flowers were thawed and dried in an incubator at 37 °C for 24 hours to facilitate pollen release from the anthers. After drying, flowers were brushed over food strainers to separate pollen from anthers and sifted through multiple sieves of decreasing mesh size (mesh sizes from 250 to 45 µm). Collection of nectar from flowers was performed *in situ* through capillary action into glass micropipettes and, once filled; both ends were sealed with putty. Samples were pooled to obtain the volume needed for analysis (50 µl/sample). Pollen and nectar samples were collected from wild flowers in the field margins using a similar technique. To collect pollen from foraging honeybees, one hive was placed in the vicinity of wOSR fields at each farm at the beginning of the flowering period (May 2013) and remained at the same sites until the end of August 2013. The hives were equipped with pollen traps during four consecutive d at the beginning of June 2013 and for four d in mid-August 2013 to collect pollen loads from the returning honey bee foragers during the wOSR blooming period, and also when no OSR was in flower. After 4 d, the traps were removed and the pollen loads were stored on ice and then at −80°C in the laboratory until analysis. Pollen loads within each sample were sorted by eye according to color, texture, size, and shape as indicators of different pollen types. All pollen types were separately weighed to calculate their relative abundance within the samples. A representative sample of loads from each pollen type was mounted,	**1**

Responses 1-6: Quality of methods		Score
	and pollen grains were identified under a microscope following standard methods and using reference specimens and published reference collections. Pollen and nectar samples were stored at -80°C prior to pesticide extraction and analysis. Analyses were performed within 10 months after collection. Transport and storage blanks and spikes were not reported but the storage conditions appear to be appropriate and this was not identified as a weakness. Analysis was well described in the paper and the SI. Samples were extracted using the QuEChERS method and analysis was by Ultra-high-performance liquid chromatography and tandem mass spectrometry (UHPLC−MS/MS). The LOQs in nectar and pollen for TMX were 0.3 and 0.36 µg/kg respectively (SI Table S5a). Recovery (SD) from nectar and pollen for TMX was 111% (5) and 95% (3), respectively (SI Table S5b). Although TMX was detected in pollen of wild-flowers at concentrations up to 86 µg/kg (Table S2d), its metabolite clothianidin was not detected in any of the samples of nectar or pollen from wildflowers in margins of wW and wOSR (Tables S2a–S2j & S3a-S3b). Clothianidin was detected in pollen and nectar from wOSR (Table 2) so this is a *weakness* that was not discussed by the authors. Statistical methods were described but some of the data were incorrectly analyzed (*weakness*). The data were shown to not be normally distributed but arithmetic means and SDs were presented. The only useful data provided was the median (*weakness*). Upper centiles were not provided. Transformation of data between the MDL and MQL would have biased the arithmetic means. Data for pollen and nectar from wOSR and were taken from Table 2 as were data for pollen collected by bees. The data for pollen from wildflowers in field margins were taken from SI Tables S2a – S2j and for nectar from Tables S3a-S3b. Medians and centiles were calculated from the raw data. Each measure was treated as independent.	
Use of GLP and QA/QC	This was not a GLP study and the QC was limited to the analysis.	**2**
Transparency of data	Raw data for concentrations of neonicotinoids in pollen and nectar from the field margins were provided but not for wOSR or pollen collected by bees. Data were presented as summary values in graphs and Tables.	**2**
Number of samples and replication	There were five sites with seven reps for pollen and nectar of wOSR and 5 for wW. For the samples of pollen and nectar from wildflowers in margins, there were 5 reps for wOSR and wW.	**4**
Duration of study sufficient to observe trends	The period of flowering for the wild plants was not reported but sampling began in Jun 2013 and was completed in Aug 2013. Most samples were taken in Jul and Aug. Since the wOSR and wW were planted in 2012, it is surprising that wildflowers did not flower until Jul-Aug the following year. It appears that the period of sampling would have missed many species of spring flowering plants.	**2**
Overall evaluation of methods	Computed mean of above	**2.2**
Score for expert judgment on Quality of the study.	**1**	**2.20**

Relevance

Hazard quotients for exposures to TMX in pollen and nectar from OSR and wildflowers in field margins of OSR and WW in the UK. (Table 2, SI Tables S2a – S2j & S3a-S3b)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR 2013 UK	Pollen collected from plants max. (n = 21)	11.1	1.38	8.6	Larva	124
wOSR 2013 UK	Pollen collected from plants 50th centile (n = 21)	3.2	0.40	8.6	Larva	124
wOSR 2013 UK Jun	Pollen collected by bees max. (n = 34)	1.8	0.22	8.6	Larva	124
wOSR 2013 UK Jun	Pollen collected by bees 50th centile (n = 34)	0	0.00	8.6	Larva	124
wOSR 2013 UK Aug	Pollen collected by bees max. (n = 46)	0.3	0.04	8.6	Larva	124
wOSR 2013 UK Aug	Pollen collected by bees 50th centile (n = 46)	0	0.00	8.6	Larva	124
wOSR 2013 UK	Nectar collected from plants max. (n = 13)	13.3	3.88	8.6	Adult	292
wOSR 2013 UK	Nectar collected from plants 50th centile (n = 13)	0	0.00	8.6	Adult	292
Wild flowers from margins of wOSR and wW 2013 UK	Pollen collected from plants 90th centile (n = 95)	40	4.96	8.6	Larva	124

Hazard quotients for exposures to TMX in pollen and nectar from OSR and wildflowers in field margins of OSR and WW in the UK. (Table 2, SI Tables S2a – S2j & S3a-S3b)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Wild flowers from margins of wOSR and wW 2013 UK	Pollen collected from plants 50th centile (n = 95)	0	0.00	8.6	Larva	124
Wild flowers from margins of wOSR and wW 2013 UK	Nectar collected from plants 90th centile (n = 28)	0	0.00	8.6	Adult	292
Wild flowers from margins of wOSR and wW 2013 UK	Nectar collected from plants 50th centile (n = 28)	0	0.00	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in pollen collected from wOSR plants resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in pollen collected from foraging bees near wOSR plants in June resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in pollen collected from foraging bees near wOSR plants in Aug resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in nectar collected from wOSR flowers resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX measured in pollen collected from wild-flowers in the margins of wOSR and WW fields resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX measured in nectar collected from wild-flowers in the margins of OSR and WW fields resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 8, 2016
SEJ	Yes	May 29, 2016

Narrative

It is surprising that TMX was detected on many occasions in pollen from wildflowers (Tables S2a–S2j) but only once in nectar from the same plants sampled on the same day (Tables S3a-S3b). The reason for this discrepancy was not discussed by the authors.

(Codling et al. 2016)
Paper: Codling G, Al Naggar Y, Giesy JP, Robertson AJ. 2016. Concentrations of neonicotinoid insecticides in honey, pollen and honey bees (*Apis mellifera* L.) in central Saskatchewan, Canada. *Chemosphere* 144:2321-2328.

This paper described the analysis of honey and pollen samples collected from beehives in Saskatchewan (Canada). Several neonicotinoids were analyzed for; only the results for TMX are presented here.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in August 2013 at the end of the nectar flow in flowers. Food plants were estimated from plants observed in a 10-km radius of the apiaries but identification was not confirmed by pollen analyses (*potential weakness*). Collection of the samples was described but no indication of measures to avoid cross-contamination was provided. Samples of honey were collected from the comb as were samples of pollen. It appears that only single samples were taken. Samples were stored in a cooler after collection and during transport to the laboratory for analysis. Temperature and duration in the cooler were not reported and the use of field spikes and blanks was not reported (***major weakness***). Samples were stored in the laboratory at -20°C (OK) but duration of storage was not reported (*potential weakness*). Extraction and analysis were reasonably well described. Blanks for pollen, honey, and bees were mentioned in the text but no details as to source were provided (*potential weakness*). Extraction was via a modified QuEChRS method. Isotopically labelled standards of imidacloprid (IMI) and clothianidin (CTD) of unreported purity were used but not for TMX. Certified standards of all neonicotinoids were used but purity was not reported. Analysis of the extracts was by HPLC MS/MS. Based different ions, the instrumental LOQs for TMX were 2 and 1 µg/L (SI Table 1) but the LOQ of the entire method was not reported (*weakness*). Identification of the neonicotinoids was judged to be well conducted but mean recoveries of isotopically labelled IMI for pollen and honey were only 61% and 68%, respectively Recovery for the other neonicotinoids was not reported and variance was not calculated (*weakness*). How these recoveries were used (i.e., correction of analytical values) was not reported (*weakness*) and how this was applied to TMX is uncertain (*potential weakness*). Exposures of bees were measured and TMX was not detected in any sample. Hazards to bees were calculated based on LD50s reported in the literature (Table 2) but the actual exposures used in the calculation were not clearly reported.	**1**
Use of GLP and QA/QC	The study was not conducted under GLP and the use of QC samples was not reported. The protocol was reasonably well described for the analysis but the field component was lacking.	**1**
Transparency of data	Raw data were not provided, even in the SI. Summary data were presented in a figure (Fig. 2). Variance was not calculated.	**1**

Responses 1-2: Quality of methods			Score
Number of samples and replication	Three samples of honey and three of pollen were taken from separate hives at each of seven sites. However, it appeared from Fig. 2 that more samples of honey were taken than pollen. The text stated that "In total 26 samples of honey, 19 of pollen and 16 of worker bees were analyzed".		**3**
Duration of study sufficient to observe trends	The study took place in August with only one sampling event. Acceptable for general trends but no temporal sampling.		**2**
Overall evaluation of methods	Computed mean of above		**1.6**
Score for expert judgment on Quality of the study. One major weakness; lack of field blanks and spikes.		**0.5**	**0.80**

Relevance

Hazard quotients for maximum concentrations of ΣTMX in pollen and honey from beehives in Saskatchewan Canada (estimated from data in Fig. 2)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Honey from hive	Honey (max.) n = 30	109	32	8.6	Adult	292
Pollen from hive	Pollen (max.) n = 21	229	29	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentrations of TMX measured in honey collected from hives in Saskatchewan was >NOAED honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentrations of TMX measured in pollen collected from hives in Saskatchewan >NOAED for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Expert judgment		
QA	Yes	April 9, 2016
SEJ	Yes	May 29, 2016

Narrative

The relevance of the exceedances in honey and pollen would still have applied if a NOAED of 14.3 ng/bee/d had been used instead of 8.6 ng/bee/d.

(David et al. 2016)
Paper: David A, Botías C, Abdul-Sada A, Nicholls E, Rotheray EL, Hill EM, Goulson D. 2016. Widespread contamination of wildflower and bee-collected pollen with complex mixtures of neonicotinoids and fungicides commonly applied to crops. *Environment International* 88:169-178.

This paper reported on concentrations of neonicotinoids in bee-collect pollen and pollen from wildflowers in the UK. Only the data for the honeybee and TMX are reported here.

Responses 1-3: Quality of methods for studies in pollen from wOSR		Score
Experimental design and hypotheses	This study was conducted in East Sussex in 2013. Pollen was collected from oil seed rape (OSR) from three farms selected for the study. The histories of pesticide use in the fields were known and clothianidin was used in Mar of 2012 (Table 1). No other neonicotinoids were used. In 2012, the seeds from the OSR fields were all treated with Cruiser® seed dressing (active ingredients (a.s.): 280 g/L TMX, 8 g/L fludioxonil and 32.2 g/L metalaxyl-M). Date of planting was not reported and analyses of soil samples were not conducted to determine historical residues (*weakness*). The seeds were not analyzed to confirm the rate of application of TMX (*weakness*). Weather conditions were not reported (*weakness*). To collect pollen from OSR, flowers were gathered, stored on ice in coolers in the field and then were frozen immediately at −80°C until further handling. After an unreported time in storage (*potential weakness*), samples of flowers were defrosted and dried in an incubator at 37°C for 24 h to facilitate pollen release. Flowers were then brushed over food strainers to separate pollen from anthers and sifted through multiple sieves of decreasing pore sizes (pore sizes from 250 to 45 μm) to isolate the pollen. To sample pollen collected by honeybees, five hives of unspecified size and origin (*weakness*) were placed at distances from 1 to 260 m from the edge of the OSR fields at the beginning of the flowering period (May 2013) until the end of Aug 2013. Collection of pollen from the bees was via pollen traps operated for four consecutive days at the beginning of June 2013 and in mid-Aug 2013 (when no wOSR was in flower). Pollen was removed at the end of sampling and stored on ice in coolers in the field, and then at −80°C until analysis. Samples of pollen from each hive were kept separately. Pollen loads within each sample were sorted by color and weighed. Pollen grains associated with plant species were identified microscopically using standard methods[9]. Use of field and transportation blanks and spikes were not reported (*weakness*). Extractions and analysis were well described. The method of analysis was adapted from a published method[10]. Certified standards (>99% pure) were used and isotopically labelled TMX and clothianidin (>97% pure) were used as internal standards. Analysis	**2**

[9] Moore, P.D., Webb, J.A., Collinson, M.E., 1991. Pollen Analysis. Wiley-Blackwell, Oxford (216 pp.).
[10] David, A. Botías, C. Abdul-Sada, A., Goulson, D., Hill, E.M., 2015. Sensitive determination of mixtures of neonicotinoid and fungicide residues in pollen and single bumblebees using a scaled down QuEChERS method for exposure assessment. Anal. Bioanal. Chem. 407, 8151–8162.

Responses 1-3: Quality of methods for studies in pollen from wOSR			Score
	was by UHPLC-MS/MS. The LOQ for pollen was 0.36 µg/kg (Table S2). Percent recovery and variance was not reported (*weakness*).		
Use of GLP and QA/QC	This was not a GLP study but the protocol was provided. There was limited QA and QC.		**1**
Transparency of data	Raw analytical data were provided in the SI.		**3**
Number of samples and replication	Samples were collected from seven fields at one to three sites (n = 11).		**4**
Duration of study sufficient to observe trends	It appears that only one sample was collected from each site but the time of flowering was from the end of May–June 2013.		**1**
Overall evaluation of methods	Computed mean of above		**2.2**
Score for expert judgment on Quality of the study.		**1**	**2.20**

Relevance

Hazard quotients for concentrations of ΣTMX in pollen from wOSR flowers and bees in the UK Tables S3, S6 and S7)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR flowers	Pollen (90th centile) n = 11	20.9	2.6	8.6	Larva	124
Honeybees during bloom of wOSR	Pollen from wOSR (max.) n = 5	0	0	8.6	Larva	124
	Pollen from other plants (max.) n = 5	1.6	0.2	8.6	Larva	124
Honeybees after bloom of wOSR	Pollen from other plants (max.) n = 5	0	0	8.6	Larva	124

Where CTD was measured in the matrix, the amount of CTD was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX. Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from flowers of wOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen of wOSR grown from seeds treated with TMX and other flowers collected by bees during bloom resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen flowers other than wOSR collected by bees after bloom resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Responses 4-5: Quality of methods for studies in pollen from wild plants in field boundaries.		Score
Experimental design and hypotheses	This study was conducted in East Sussex in 2013. In addition to the studies on wOSR described above, three farms were selected for the study of uptake and translocation of CTD used as a seed dressing for winter wheat (WW) into wild flowers. The histories of pesticide-use in the fields were known and TMX was used in Aug 2011 (Table 1). No other neonicotinoids were used. In 2012, the seeds from the ww fields were all treated with treated with Redigo® Deter® (a.s.: 50 g/L prothioconazole and 250 g/L clothianidin). Date of planting was not reported and analyses of soil were not conducted to determine historical residues (*weakness*). The seeds were not analyzed to confirm the rate of application of CTD (*weakness*). Weather conditions were not reported (*weakness*). Pollen for wildflowers was sampled from the field boundaries of the wOSR and WW fields. Field boundaries in the region consisted of a hedge of woody plants separated from the crop by a 0–2 m strip of herbaceous vegetation. The average sample distance from the crop edge was 1.5 m (range 1–2 m). Samples were collected from four of the seven wOSR fields as well as in the margin of four WW fields on the same three farms. Samples of pollen were collected from the wildflowers using the method described above for OSR plants. The species of wildflowers collected depended on availability. Wildflowers were identified using a visual identification guide. In OSR field margins, pollen from eight different wildflowers comprising four different species (*Ranunculus repens*, *Silene latifolia* (collected three times), *Matricaria recutita* (collected three times), *Cirsium vulgare*). In margins of WW fields, pollen from 13 wildflowers comprising six different species (*Heracleum sphondylium* (collected five times), *Papaver rhoeas*, *Senecio jacobaea* (collected twice), *Pimpinella saxifraga, Aethusa cynapium* and *M. recutita* (collected three times)) was collected. Pollen samples were analyzed separately for each species of wildflower, except where amounts <20 mg of four wildflower pollen samples collected from plants growing at the same site of a WW field margin, which were pooled and analyzed as a single sample. It is assumed that the samples of pollen were collected, transported, and stored as for response 1-3. Field and transportation blanks and spikes were not reported used (*weakness*) Extractions and analysis were well described. The method of analysis was adapted from a published method[10]. Certified standards (>99% pure) were used and isotopically labelled TMX and clothianidin (>97% pure) were used. Analysis was by UHPLC-MS/MS. The LOQ for pollen was 0.36 µg/kg (Table S2). Percent recovery and variance was not reported (*weakness*).	**2**

Responses 4-5: Quality of methods for studies in pollen from wild plants in field boundaries.			Score
Use of GLP and QA/QC	This was not a GLP study but the protocol was provided. There was limited QA and QC.		**1**
Transparency of data	Raw analytical data were provided in the SI.		**3**
Number of samples and replication	Samples were collected from seven fields at one to three sites (n = 11).		**4**
Duration of study sufficient to observe trends	It appears that only one sample was collected from each site but the time of flowering was from the end of May–June 2013.		**1**
Overall evaluation of methods	Computed mean of above		**2.2**
Score for expert judgment on Quality of the study.		**1**	**2.20**

Relevance

Hazard quotients for concentrations of ΣTMX in pollen from wild flowers in field margins of OSR (Table S4) and WW (Table S5)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Wild flowers in wOSR margins	Pollen (max.) n = 8	21	2.6	8.6	Larva	124
Wild flowers in WW margins	Pollen (max.) n = 10	6.3	1	8.6	Larva	124

Where CTD was measured in the matrix, the amount of CTD was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX. Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from wild-flowers in the margins of fields planted with wOSR treated with TMX resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from wild-flowers in the margins of fields planted with wOSR treated with CTD resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 9, 2016
SEJ	Yes	May 29, 2016

(Dively and Kamel 2012)
Paper: Dively GP, Kamel A. 2012. Insecticide residues in pollen and nectar of a cucurbit crop and their potential exposure to pollinators. Journal of Agricultural and Food Chemistry 60:4449-4456

This study measured levels of neonicotinoid residues in pollen and nectar from a pumpkin crop treated with foliar applications of formulated products containing imidacloprid (Admire Pro®), dinotefuran, thiamethoxam (Platinum®), and oxamyl using different timings and application methods. Only the data for TMX are included in this WoE.

Responses 1-12: Quality of methods		Score
	The study was repeated over two years, 2009 and 2010 in Beltsville, MD, USA. The crop was pumpkin (*Cucurbita pepo* L. var. 'Howden'). Seedling plants were grown from untreated seed in a greenhouse and then transplanted onto plastic mulch beds in early June of each year. A replicate treatment plot consisted of a single row containing 18 plants spaced according to local commercial practices but treatments were separated with greater distance apart. Treatment plots were arranged in a randomized complete block design with four replicates. Fertilizer was applied to the plots prior to laying the plastic mulch and provided with additional nitrogen via chemigation. Chlorothalonil (Bravo; Helena Chemical Co) was applied during the crop cycle to control leaf diseases. The 2009 study included the following treatments: 7) Split treatments of TMX (Platinum, 21.6% a.s.; Syngenta Crop Protection) applied as a half rate (96 g a.s./ha) in transplant water and the remaining half rate applied three weeks later by drip irrigation. 8) Two foliar treatments of TMX (Actara, 25% a.s.; Syngenta Crop Protection), each 96 g a.s./ha, at 4 and 6 weeks after transplanting 9) Untreated control. It is not clear if the plots had been previously treated with TMX. Soils were not analyzed and 38% of the samples from the control plots had detectable residues of TMX suggesting cross-contamination or prior treatment (***major weakness***). In 2010, the same treatments were used except that treatment 3 was omitted and two additional treatments with oxamyl were added. In addition, a seed dressing which delivered 0.75 mg a.s. of thiamethoxam per seed (4.5 g AS/ha) and three fungicides (fludioxonil, mefenoxam, azoxystrobin) were investigated. This treatment was direct-seeded by hand into plots 10 d prior to the establishment of the other plots. **This was the only study included in the QWoE as it was a seed treatment.** In 2009 and 2010, transplant treatments were applied by drenching 0.25 L of solution around each seedling immediately after transplanting. Foliar treatments were applied with a CO_2 backpack sprayer. Drip treatments were applied using CO_2 pressure to first force 8 L of water through the drip line to prime emitters, followed by 8 L of the treatment solution, and then 8 L of water to flush out the line. Transplant and drip treatment rates were based on a plant population of 5,977/ha, typical of a commercial field.	**3**

Responses 1-12: Quality of methods		Score
	During flowering (≈ 5 weeks after transplanting), pollination bags were secured over unopened flower buds that had not yet bloomed to prevent pollinator visits. Bags with open flowers were removed the following day and brought to the laboratory to extract nectar and pollen. The calyx and corolla were removed and nectar collected with a syringe. Multiple flowers (40−50/replicate) were sampled until 1.5 mL of nectar had been collected from each replicate. Pollen was then dislodged from the anther stalk until least 3 g per replicate was collected. Separate tools were used for each treatment, disposable gloves were changed between samples, and other undescribed measures to minimize cross-contamination were used. Sampling was repeated 2–3 times over a period of 7−10 d to obtain sufficient quantities for analysis. The pooled samples represented the average concentration during the collection period. For foliar applications in 2010, separate samples of nectar and pollen were collected after each application of TMX. Samples of leaves were analyzed but are not included in this assessment. All samples were stored in 15 mL centrifuge tubes at −80°C until ready for residue analysis. Controls (field blanks) were used. Analysis was well described. Standards were >98.9% pure and ^{13}C-d^3-IMI was used as an internal standard. Analysis was by LC MS/MS. The LOD for TMX was 0.2 µg/kg and 0.2 to 3 µg/kg for the biologically relevant metabolites (clothianidin). The LOQ was estimated as 3.33 times the LOD. Recovery was not stated; however, quantitation was based on the internal standard. RSD was <20%. Centiles of values were not reported. Statistical methods were described. ANOVA procedures were used to test for significant differences between residues methods of application.	
Use of GLP and QA/QC	Not a GLP study but some QA on the collection of nectar and pollen. Protocol and analysis described in detail.	**1**
Transparency of data	Raw data were not provided. Mean, max. and min. values were provided and statistical tests were used to differentiate results of treatments; however, data on variance were not provided. Metabolites TMX were reported but could not be added to the parent as raw data were not provided except for the mean values (weakness).	**1**
Number of samples and replication	Four replicates of each treatment and most parts of the study were repeated in the following year. Given the study design, pooling samples within replicates is acceptable,	**2**
Duration of study sufficient to observe trends	Sampling of flowers was for up to 10 d, less than the total flowering period but close to initiation of flowering when residues would be expected to be greatest.	**1**
Overall evaluation of methods	Computed mean of above	**1.6**
Score for expert judgment on Quality of the study. Large number of detects of TMX in control plots identified as a **major weakness.**	**0.5**	**0.80**

Relevance

Hazard quotients for exposures to TMX in honey bees via pollen and nectar from pumpkin (data from Tables 1-4)

Source	Matrix	Conc. TMX µg/kg	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg of food or water/d
Pumpkin seed treat. 2010	Nectar min	0.1	0.03	8.6	Adult	292
Pumpkin seed treat. 2010	Nectar mean ΣTMX	0.2	0.06	8.6	Adult	292
Pumpkin seed treat. 2010	Nectar max	0.1	0.03	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value exceeds toxicity value	The maximum concentrations of TMX in nectar from seed-treated pumpkin in 2010 resulted in exposures that were all less than the NOAED		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 8, 2016
SEJ	Yes	May 29, 2016

Narrative

Some post-transplant applications of TMX as a drip or foliar application resulted in exposures greater than the NOAED but these were not included in the WoE. Other methods of application did not result in concentrations >NOAED.

(Henry et al. 2015)
Paper: Henry M, Cerrutti N, Aupinel P, Decourtye A, Gayrard M, Odoux J-F, Pissard A, Rüger C, Bretagnolle V. 2015. Reconciling laboratory and field assessments of neonicotinoid toxicity to honeybees. *Proceedings of the Royal Society B Biological Sciences* 282:20152110.

This study was conducted to assess the effects of exposure of honeybee colonies to neonicotinoid insecticides under field conditions on the structure of the hive. As part of this study, concentrations of TMX were measured in honey. These data are assessed here.

Response 1: Quality of methods			**Score**
Experimental design and hypotheses	The study was conducted in France in the LTER Zone Atelier Plaine & Val de Sévre area. Oilseed rape seeds coated with the Cruiser® formulation (280 g/L but actual rate on the seeds was not reported and treatment concentration not measured (*weakness*)) were planted in fields totaling 153 ha in 2013 and 135 ha in 2014. Eighteen standardized experimental colonies bred from sister queens were set up in 10-frame Dadant hives at various distances from the treated fields. During bloom of OSR, 200 forager bees were collected for extraction of nectar. Three samples were taken at 7-d intervals. Bees were anaesthetized with di-ethyl ether in a cage and nectar was collected from the honey-stomach by compression of the abdomen. Samples of nectar from individual bees were pooled in Eppendorf tubes. Storage conditions for the samples were not reported (*weakness*). Field blanks and spikes and transport and storage spikes were not reported (*weakness*). Analysis of pollen was not undertaken and sources of pollen were not characterized (*weakness*). Other than the statement that the analysis was by a multi-residue method, details of the extraction procedures, internal standards, recovery, LOD, and LOQ were not reported (***major weakness***). The relationship of the data in the graph (Fig. S2A) was not characterized except for an apparent linear regression but no parameters or correlation-coefficient were calculated or provided (*weakness*). Frequency of non-detects was not reported.		**1**
Use of GLP and QA/QC	This was not a GLP study, the protocol was poorly described and QA and QC procedures were not reported,		**0**
Transparency of data	Raw data were not provided, only a scatter-graph. Centiles were not calculated.		**1**
Number of samples and replication	There were 18 hives and each was sampled three times over the two year-period.		**3**
Duration of study sufficient to observe trends	Sufficient for the objectives of the study.		**4**
Overall evaluation of methods	Computed mean of above		**1.8**
Score for expert judgment on Quality of the study. Analytical methods incompletely reported (***major weakness***).		**0.5**	**0.90**

Relevance

Hazard quotients for concentrations of TMX in nectar collected in France (data from Fig S2A and text)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives in France	Nectar collected by bees, max. (n = 18 x 3)	0.8	0.2	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in nectar collected by bees from OSR fields resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

(Jones and Turnbull 2016)
Paper: Jones A, Turnbull G. 2016. Neonicotinoid concentrations in UK honey from 2013. *Pest Management Science* 72:1897–1900

Concentrations of the neonicotinoid insecticides clothianidin, thiamethoxam (TMX) and imidacloprid were determined in honey collected in Spring 2013 from a variety of locations in the UK. The honey was produced before the moratorium in the EU on the use of neonicotinoids in pollinator-attractive crops became effective and was focused on oilseed rape, the crop with the major use of neonicotinoids.

Response 1: Quality of methods			**Score**
Experimental design and hypotheses	Honey samples produced from known apiaries were collected in early Spring 2013 by Regional Bee Inspectors employed by the Department for Environment, Food and Rural Affairs (Defra) from a range of locations. Inspectors also determined whether the apiaries were within approximately 3 km of an oilseed field (OSR) during 2012. No details on the collection, transport, and storage of the samples of honey were provided (***major weakness***). Field blanks and transport and storage spikes were not reported (*weakness*). Measures to avoid contamination were not reported (*weakness*). Extraction and analysis of the honey were well described. Analysis was by LC-MS/MS operated in positive electrospray mode. Laboratory control samples were used to check for recovery but it appeared that isotopically labelled internal standards were not used. The LOD for TMX was 0.01 µg/kg and for clothianidin was 0.02 µg/kg. Recovery for TMX was 99 and 91% and for clothianidin was 97 and 101%. Variance was not reported.		**2**
Use of GLP and QA/QC	Not a GLP study. Protocol for collection was not provided. Some QA in the analysis.		**1**
Transparency of data	Raw data were provided		**4**
Number of samples and replication	There were 22 independent sites with one replicate each.		**4**
Duration of study sufficient to observe trends	Duration was appropriate to the design of the study.		**4**
Overall evaluation of methods	Computed mean of above		**3**
Score for expert judgment on Quality of the study. One **major weakness**, lack of storage spikes, identified**.**		**0.5**	**1.50**

Relevance

Hazard quotients for concentrations of ΣTMX in honey collected in the UK (data from Table 3)

Source of matrix	**Sample**	**Conc. ΣTXM in µg/kg or L**	**Dose ng/bee**	**Chronic NOAED ng/bee/d**	**Life-stage**	**mg diet/d**
Hives in the UK	Honey (90th centile) n = 22	1	0.3	8.6	Adult	292

Where CTD was measured in the matrix, the amount of CTD was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX. Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of ΣTMX measured in honey resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 10,2016
SEJ	Yes	May 29, 2016

(Kasiotis et al. 2014)
Paper: Kasiotis KM, Anagnostopoulos C, Anastasiadou P, Machera K. 2014. Pesticide residues in honeybees, honey and bee pollen by LC-MS/MS screening: reported death incidents in honeybees. The Science of the Total Environment 485-486:633-642.

The aim of this paper was to investigate deaths of bees in several areas of Greece. A method of analysis was developed and some samples were analyzed. As the samples were not taken at random and focused on incidents, they are not representative of typical exposures. However, the data were included in the WoE analysis with a caveat. Only data for TMX were assessed.

Responses 1-3: Quality of methods			**Score**
Experimental design and hypotheses	The method of analysis was well described but sample collection was poorly described. Control samples of honeybees, bee pollen and honey were obtained from beehives used for organic apiculture. The investigated samples were collected by individuals or public authorities who observed incidents of bee death. Bees were collected very near or at the entrance of the hives; pollen was collected from the hives. No description of the collection of honey was provided (weakness). Other than cooling the samples with ice or dry-ice, no details of the collection procedures or avoidance of contamination were provided and control samples (field blanks) were not collected at the same time as the test samples (**major weakness**). After arrival at the laboratory, the samples were stored at −20°C until analysis. Isotopically labelled standards were not used (potential weakness). The analytical methods were clearly described and used a Triple Quad LC/MS for quantitation. Certified standards were obtained from a commercial supplier and were >90% pure; however, data for individual compounds were not provided. LOD for TMX was 0.06 µg/kg; LOQ was 0.2 µg/kg. Recovery ranged from 73 to 80% and RSDs from 6 to 10% (Table 3). Individual analytical data for the samples were provided in SI Table S12. Statistical analysis was not reported.		**2**
Use of GLP and QA/QC	Not a GLP study. Protocol provided but lacking some detail. Some QC on the analysis but no QA on field samples.		**1**
Transparency of data	Raw data were provided in SI.		**4**
Number of samples and replication	Several sites (>10) were sampled and some included multiple samples (from 1 to 5).		**3**
Duration of study sufficient to observe trends	The study began in 2011 and ended in July 2013, duration sufficient for the objectives of the study.		**4**
Overall evaluation of methods	Computed mean of above		**2.8**
Score for expert judgment on Quality of the study That control samples (field blanks) were not collected at the same time as the test samples was identified as a (***major weakness***).		**0.5**	**1.40**

Relevance

Hazard quotients for exposures to TMX in honey bees via pollen from and honey from hives and concentrations measured in bees. All samples from hives with suspected poisoning (SI Table S12).

Source	Matrix	Conc. TMX µg/kg	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg of food or water/d
Greece 2011-2013	Pollen from hive, median	0	0.0	8.6	Larva	124
Greece 2011-2013	Pollen from hive, 90th centile	0	0.0	8.6	Larva	124
Greece 2011-2013	Honey from hive, median	0	0.0	8.6	Adult	292
Greece 2011-2013	Honey from hive, 90th centile	0	0.0	8.6	Adult	292
Greece 2011-2013	Conc. in bee, median	0	0.0	8.6	Adult	NA
Greece 2011-2013	Conc. in bee, 90th centile	0	0.0	8.6	Adult	NA

Assumed that a bee weighs 100 mg, conversion to dose in ng/bee is µg/kg bee/10

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects from exposure to TMX in pollen.			**Score**
Comparison of exposure value exceeds toxicity value	The 95th centile concentrations of TMX in pollen resulted in exposures that were all less than the NOAED		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects to TMX in honey.			**Score**
Comparison of exposure value exceeds toxicity value	The 95th centile concentrations of TMX in honey resulted in exposures that were all less than the NOAED		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects from exposure to TMX in pollen.		**Score**
Comparison of exposure value exceeds toxicity value	The 95th centile concentrations of TMX in bees resulted in exposures that were all less than the NOAED	**0**

Response 3: Relevance to adverse effects from exposure to TMX in pollen.			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 9, 2016
SEJ	Yes	May 29, 2016

(Krupke et al. 2012)
Paper: Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple routes of pesticide exposure for honey bees living near agricultural fields. PLoS ONE 7:e29268.

This paper reported on several measurements of exposure concentrations of CTD and TMX in honeybee-relevant matrices associated with the planting of maize seeds treated with these neonicotinoids and other pesticides. Some exposures were related to contamination with soil-dust and seed-dust from planting but also to uptake from treated seeds or from residues present in soil. It was not possible to distinguish these in the study so the data were pooled.

Response 1-2: Quality of methods for analysis of concentrations of TMX in pollen from maize plants from fields planted with treated and untreated seed.		**Score**
Experimental design and hypotheses	The experiment took place at Purdue Agricultural Center, Indiana, USA. The experimental field was surrounded by fields planted with maize and soybeans. The field was 142 x 148 m. Half the field was planted with seed containing 1.25 mg CTD per seed (not analyzed; *weakness*). The other half was planted with untreated seed. Talc was added to the seeds as a lubricant. The proximity of these fields was a ***major weakness***. The fields were planted on July 12 2010 when the surrounding corn fields were in tassel stage and a combination of dust from the planters and the soil presumably contaminated the adjacent fields. This is not the normal time for planting of corn and the conditions would likely not be appropriate. Previous and current use of pesticides in the test and surrounding fields was not reported (*weakness).* Wind direction and velocity were not reported (*weakness)*. Samples of fresh pollen from maize anthers were taken by removing the entire tassel from approximately 100 plants in the field while pollen was being shed. The tassels were vigorously shaken into paper bags. The resulting mixture of pollen and anthers was spread over paper towels. Anthers and other large debris were removed so that only pollen grains remained for analysis. No information was provided on measures to prevent contamination (weakness). Soil samples were taken in the fields and the margins and no TMX was detected in analyses (data not discussed in this WoE). After collection, samples were held at -10°C prior to analysis. This is less than the -18°C on which the stability in storage was based. Date of analysis was not provided so it was not possible to judge the time of storage before analysis. As no transport and storage spike samples were used, this is a ***major weakness****.* Analysis of samples used the QuECHeRs method and the method of extraction was described. Analysis was by LC/MS/MS. Purity of standards and recovery of the method was not reported (*weakness*). LOD for TMX in pollen and nectar 0.2–0.5 µg/kg (Tables 3-5).	**1**
Use of GLP and QA/QC	The study was not conducted under GLP and there was no reporting of QA and QC. The protocol was incomplete several aspects were not reported.	**1**
Transparency of data	Raw data for analysis were provided in Table 3.	**4**
Number of samples and replication	There was one site and one replicate of the experimental field.	**1**

Response 1-2: Quality of methods for analysis of concentrations of TMX in pollen from maize plants from fields planted with treated and untreated seed.			**Score**
Duration of study sufficient to observe trends	Only one sample was taken duration of the study was judged to be inappropriate for the objective of the study.		**1**
Overall evaluation of methods	Computed mean of above		**1.6**
Score for expert judgment on Quality of the study. Lack of transport and storage spike samples judged as a **major weakness** because of the lack of storage of samples at temperatures ≤-18°C. Proximity of fields was identified as a major weakness.		**0.25**	**0.40**

Response 3-6: Quality of methods for analysis of concentrations of TMX in pollen collected by honeybees from maize and other plants adjacent to fields planted with treated and untreated seed.		**Score**
Experimental design and hypotheses	The experimental field was the same as above. Eight beehives each contain 20,000 to 30,000 bees were placed such that each field-half had a hive in the center of each border. Hive entrances faced the field interior. Pollen traps were placed in the entrances of each hive and pollen samples collected daily both before and after the field was planted. The length of time the traps were in place was not stated but they pollen was collected on day of planting and two d before and after planting (Table 4). It is not clear why results were reported from only 4 hives when eight were reported used (weakness). Soil samples were taken in the fields and the margins no TMX was detected in analyses (data not discussed in this WoE). After collection, samples were held at -10°C prior to analysis. This is less than the -18°C on which the stability in storage was based. Date of analysis was not provided so it was not possible to judge the time of storage before analysis. As no transport and storage spike samples were used, this is a ***major weakness***. Source of the pollen was determined by microscopic identification. Analysis of samples used the QuECHeRs method and the method of extraction was described. Analysis was by LC/MS/MS. Purity of standards and recovery of the method was not reported (*weakness*). LOD for TMX in pollen and nectar was 0.2–0.5 µg/kg (Tables 3-5).	**1**
Use of GLP and QA/QC	The study was not conducted under GLP and there was no reporting of QA and QC. The protocol was incomplete several aspects were not reported.	**1**
Transparency of data	Raw data for analysis were provided in Table 4.	**4**
Number of samples and replication	There was one site and four pseudoreplicated hives in the experimental field.	**1**
Duration of study sufficient to observe trends	Five samples were taken in total with three representing planting and 2-d post-planting. This was judged to be appropriate for the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**2.2**
Score for expert judgment on Quality of the study. Lack of transport and storage spike samples was judged as a major weakness because of the lack of storage of samples at temperatures ≤-18°C.	**0.5**	**1.10**

Response 7-9: Quality of methods for analysis of concentrations of TMX in dead honeybees, pollen, and nectar from hives where mortality was observed.		**Score**
Experimental design and hypotheses	This was an observational study carried out in 2011 in response to the observation of dead bees at a local apiary, located in a small wooded area near maize and soybean production fields in northwestern Indiana. These reports coincided with local planting (unreported crops and unreported pesticide treatments) and tillage activities (undescribed). Bees were collected from the entrances of several hives on May 10th and 12th, 2011. The preparation of samples of bees was not reported so it is unclear whether the residues were on the skin, in the pollen, or in the body (***major weakness***). For this reason, the analyses of bees were not included in the WoE. Apparently healthy returning foragers from hives at the same apiary were also collected for analysis. Nectar and pollen were collected from a hive with dead bees near its entrance and from a nearby hive without any dead bees visible. Storage and transport conditions were not reported. Date of analysis was not provided so it was not possible to judge the time of storage before analysis. As no transport and storage spike samples were used, this is a ***major weakness***. Analysis of samples used the QuEChERS method and the method of extraction was described. Analysis was by LC/MS/MS. Purity of standards and recovery of the method was not reported (*weakness*). LOD for TMX in pollen was 0.2–0.5 µg/kg (Tables 3–5). No TMX was detected in the bees from the "healthy" hive or in the nectar from the "healthy" and from the "sick" hive.	**1**
Use of GLP and QA/QC	The study was not conducted under GLP and there was no reporting of QA and QC. The protocol was incomplete several aspects were not reported.	**1**
Transparency of data	Raw data for analysis were provided in Table 5.	**4**
Number of samples and replication	There was one site and one hive.	**1**
Duration of study sufficient to observe trends	Six samples of bees, two of pollen and one of nectar were taken in total two days. This was judged to be inappropriate for the objectives of the study.	**2**
Overall evaluation of methods	Computed mean of above	**1.8**
Score for expert judgment on Quality of the study. Lack of transport and storage spike samples judged as a **major weakness** because of the lack of storage of samples at temperatures ≤-18°C. Lack of separation of external and internal residues was identified as a ***major weakness***	**0.25**	**0.45**

Relevance

Hazard quotients for exposures to TMX in pollen from maize adjacent to fields before and after planting with treated and untreated seed. (Tables 3-5)

Source of matrix	**Sample**	**Conc. TXM in µg/kg or L**	**Dose ng/bee**	**Chronic NOAED ng/bee/d**	**Life-stage**	**mg diet/d**
Maize from field planted with treated seeds treated with CTD	Pollen collected from plants (n = 1)	1.7	0.21	8.6	Larva	124

Hazard quotients for exposures to TMX in pollen from maize adjacent to fields before and after planting with treated and untreated seed. (Tables 3-5)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize F field planted with untreated seeds	Pollen collected from plants (n = 1)	0	0.00	8.6	Larva	124
Maize adjacent to field before planting with seeds treated with CTD	Pollen collected by bees max. (n = 2 x 2)	7.4	0.92	8.6	Larva	124
Maize adjacent to fields before planting with untreated seeds	Pollen collected by bees max. (n = 2 x 2)	0	0.00	8.6	Larva	124
Maize adjacent to fields after planting with seeds treated with CTD	Pollen collected by bees max. (n = 2 x 3)	1.2	0.15	8.6	Larva	124
Maize adjacent to fields after planting with untreated seeds	Pollen collected by bees max. (n = 2 x 3)	0	0.00	8.6	Larva	124
"Sick" hive during planting and tillage in 2011	Pollen collected by bees mean (n = 1)	20.4	2.5	8.6	Larva	124
"Healthy" hive during planting and tillage in 2011	Pollen collected by bees mean (n = 1)	6.2	0.77	8.6	Larva	124
"Healthy" and "sick" hive during planting and tillage (2011)	Nectar collected by bees, max. (n = 2)	0	0.00	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from maize plants from a field planted with seeds treated with clothianidin resulted in exposures that were >0 but less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from maize plants from a field planted with untreated seeds resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees from maize plants adjacent to a field before being planted with seeds treated	**0**

Response 3: Relevance to adverse effects			Score
	with clothianidin resulted in exposures that were >0 but less than the NOAED for bees.		
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees from maize plants adjacent to a field before being planted with untreated seeds resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees from maize plants adjacent to a field after planting with seeds treated with clothianidin resulted in exposures that were >0 but less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees from maize plants adjacent to a field after planting with untreated seeds resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 7: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from a “sick” hive during tillage and planting were >LOD but <NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 8: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from a “healthy” hive during tillage and planting were >the LOD but <NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 9: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from a “sick” and a “healthy” hive during tillage and planting were <LOD and <NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**

Score for expert judgment on relevance of the results.	**1**	**0.00**

Expert judgment		
QA	Yes	April 8, 2016
SEJ	Yes	May 29, 2016

Narrative
That exposure concentrations measured in pollen collected by bees before seeding were greater than those after seeding is counterintuitive but there is no obvious explanation other than differences in wind speed and wind direction, which were not reported.

(Mullin et al. 2010)
Paper: Mullin CA, Frazier M, Frazier JL, Ashcraft S, Simonds R, Vanengelsdorp D, Pettis JS. 2010. High levels of miticides and agrochemicals in North American apiaries: Implications for honey bee health. PLoS ONE 5:e9754.

This study was not experimental. Samples of pollen, honey, and comb wax were analyzed for residues of insecticides. Only data for TMX are included in this assessment.

Response 1: Quality of methods			**Score**
Experimental design and hypotheses	Wax from honeycomb, pollen, and bees were collected from across N. America in 2007 and 2008. Samples were not collected at random (potential weakness) and included samples taken in relation to a study on colony collapse disorder. Various individuals were involved in collection of the samples and procedures varied. Samples were maintained at low temperatures (mostly -20°C) after collection. Control (field blanks) spikes were not reported. Given the variation in the collection procedures, lack of field spikes and blanks is a **major weakness.** Pesticide residue analysis was well described and was conducted by the USDA-AMS-NSL laboratory in Gastonia, NC. A modified QuEChERS method[11] was used that was adapted for smaller 3 g samples of material. Isotopically labelled standards were not reported to be used (potential weakness). Internal standards were of the "highest purity" available but this was not stated. Analysis was by LC/MS/MS. The LOD for TMX in pollen was 5 µg/kg. Concentrations TMX were provided in author's Table 2.		**2**
Use of GLP and QA/QC	This was not a GLP study but the protocol was described; however, the descriptions were general and procedures could not be linked to individual samples. There was limited QC.		**2**
Transparency of data	Raw data were not provided in the paper or in the SI. Mean, SDs, and some centiles were provided. It is not clear how the centiles were calculated although it was stated that the concentrations <LOD were assumed to be zero. It is not clear how the authors arrived at their centiles. For example, in Table 2, residues of TMX were reported detected in only 1 of 350 samples of pollen. This value was 53 µg/kg and the other 349 samples were presumably <LOD (5 µg/kg). The median and the 95th centile should be 0, not 53 as listed in Table 2.		**1**
Number of samples and replication	It is not clear if the samples were replicated and how many were obtained from individual sites; however, the number of samples was >200, so a score of 4 was assigned.		**4**
Duration of study sufficient to observe trends	The span of the sampling for the study was 2 y but trend analysis was not conducted. Period was appropriate to the objectives of the study.		**3**
Overall evaluation of methods	Computed mean of above		**2.4**
Score for expert judgment on Quality of the study. Lack of field spikes and blanks is a **major weakness.**		**0.5**	**1.20**

[11] Lehotay SJ, Mastovska K, Lightfield AR. 2005. Use of buffering and other means to improve results of problematic pesticides in a fast and easy method for residue analysis of fruits and vegetables. J AOAC Int 88:615–629.

Relevance

Hazard quotients for exposures to TMX in honey bees via pollen (data from Table 2).

Source	Matrix	Conc. TMX µg/kg	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg of food or water/d
N. America max. (Fod = 1/350)	Pollen from hives	53	6.6	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The maximum concentration of TMX measured in pollen collected from hives in North America resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 9, 2016
SEJ	Yes	May 29, 2016

(Pacífico da Silva et al. 2015)
Paper: Pacífico da Silva I, Oliveira FAS, Pedroza HP, Gadelha ICN, Melo MM, Soto-Blanco B. 2015. Pesticide exposure of honeybees (*Apis mellifera*) pollinating melon crops. *Apidologie* 46:703-715

This paper reports analyses of TMX (and other pesticides) in honey from bees used to pollinate melons in the Rio Grande do Norte state of Brazil. Only the data for TMX and honeybees are included in this WoE.

Response 1: Quality of methods			**Score**
Experimental design and hypotheses	This study was conducted in Brazil. The date of sampling and the exact location of the hives were not reported. Honey samples were collected from 23 colonies of honeybees used to pollinate melon crops Samples were collected directly from two frames of each colony. Exact method of collection and procedures to reduce contamination were not reported (*weakness*). Storage temperature and duration of storage was not reported (*weakness*). Use of field blanks, field spikes, and transport and storage spikes was not reported (***major weakness***). No pesticides were used in the beehives to control parasites such as Varroa mites. The extraction and analysis of the samples was well described. Analysis was by UFLC-MS/MS. The purities of the standards were reported but it appeared that isotopically labelled internal standards were not used. The LOQ for all pesticides was reported as 10 µg/kg and the recoveries ranged from 70 to 120%. Although various statistical comparisons were conducted, only medians were reported. Centiles could not be calculated.		**2**
Use of GLP and QA/QC	The study was not GLP and the collection of the samples was poorly described. The analytical methods were well described but QA and QC were not reported.		**1**
Transparency of data	Raw data were not provided. Summary data were provided in Table 11.		**1**
Number of samples and replication	There was one location and apparently one site. Twenty-three hives were sampled (pseudo-replication).		**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate for the experimental design.		**4**
Overall evaluation of methods	Computed mean of above		**1.8**
Score for expert judgment on Quality of the study. Lack of field blanks, field spikes, and transport and storage spikes was identified as a (***major weakness***)		**0.5**	**0.90**

Relevance

Hazard quotients for concentrations of TMX in honey collected in Brazil from hives association with melon production (data from Table II)

Source of matrix	**Sample**	**Conc. TXM in µg/kg or L**	**Dose ng/bee**	**Chronic NOAED ng/bee/d**	**Life-stage**	**mg diet/d**
Hives in Brazil	Honey (max.) n = 23	19.1	5.6	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The max. concentrations of TMX measured in the honey collected from hives in association with production of melons resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 10, 2016
SEJ	Yes	May 29, 2016

(Pohorecka et al. 2012)
Paper: Pohorecka K, Skubida P, Miszczak A, Semkiw P, Sikorski P, Zagibajło K, Teper D, Kołtowski Z, Skubida M, Zdańska D, Bober A. 2012. Residues of neonicotinoid insecticides in bee collected plant materials from oilseed rape crops and their effect on bee colonies. Journal of Apicultural Science 56:115-134

The aim of the study was to measure the concentration of neonicotinoid insecticides (including imidacloprid, clothianidin & TMX) in nectar, pollen, honey, bee bread. This WoE is focused only on TMX. Other neonicotinoids were used as foliar sprays and are not included in the characterization of exposure. The WoE for effects is summarized elsewhere.

Responses 1-10: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in Poland at an unreported location. In **2010**, two winter oilseed rape fields (wOSR) (field A - 41 ha - and field - B 35 ha) were treated with TMX (CRUISER OSR 322 FS) and IMI (CHINOOK PLUS 500 FS) as seed dressing, respectively. In **2012**, three separate spring OSR fields (field C - 29 ha, field D - 21 ha and field E - 17 ha) were planted with OSR seed treated with TMX (CRUISER OSR 322 FS), CTD (MODESTO 480 FS), and IMI (CHINOOK PLUS 500 FS), respectively. Distances between the fields were not reported (*weakness*). All the crops were also treated with herbicides, fungicides and insecticides from other chemical classes as required by good agricultural practice. The detailed description of the products used was provided (Table 1). The blooming period of wOSR was 31 Apr to 21 May 2010. The sOSR bloomed from the 14 Jun to 2 Jul 2012. Seed was not analyzed for amount of a.s. and the rate of treatment was not reported (*weakness*). Bees used in the study were assessed for health and disease status. Ten colonies of honeybees (*Apis mellifera carnica, Apis mellifera caucasica*) were placed near each oilseed rape field, throughout the flowering period (ca. 3 weeks). In each group, an additional five hives equipped with pollen traps were designated only for collection of pollen loads. Two control groups of hives (one in 2010 and one in 2012) were in an area where no rape was grown. During flowering of rape samples of nectar were collected from rape flowers protected from insects by 16 m^2 mesh tunnels. A min. of six samples were collected from each field during the flowering period. Nectar flow from combs (100 g) was taken 7 and 14 d after the colonies were placed on the fields. Honey (100 g) was harvested separately for each colony (from honey chambers only) once, about one week after the blooming period. During the 3-week period of blooming, all of the pollen loads that the bees had collected within a 3–4-day period were taken separately from the pollen traps of each of the five colonies. Samples of bee bread (app. 10×10 cm pieces of combs) were taken once, after the blooming period. About 100 of bee workers were taken from brood chamber one time, after the oilseed rape blooming period. Samples of nectar, honey and pollen were taken for identification of source. Bees were also collected for residue analysis but were not included in this WoE. All	**3**

Responses 1-10: Quality of methods		Score
	collected samples were frozen and stored at a low temperature of about -20°C. The residue analysis was described in detail. The standard of TMX was from a commercial source and was >93.3% (typically>99%) pure. Internal isotopically-labelled standards were not used (*weakness*). Extractions followed the QuEChERS method. Analysis was by LC-MS/MS. And the analysis followed the guideline of SANCO/825/00 rev 8.1. Mean recovery efficiencies for all collected matrices were from 70-110% and the relative standard deviation was less than 20%. LOQs (Table 2) for TMX in nectar and honey were 0.5 µg/kg. In pollen and bee-bread LOQs for TMX were 1.5 µg/kg. No residues of any seed treatments were detected in nectar, honey or pollen from the controls of wOSR (Table 6) and only TMX was detected in pollen loads from the controls of sOSR (Table 7). TMX was not detected in any samples collected from field B (treated with imidacloprid) in winter rape (Table 6), but TMX was detected in samples of nectar, honey, pollen, and bee bread collected from field D (seed treated with clothianidin) and samples of nectar and honey collected from field E (seed treated with imidacloprid) for spring rape (Table 7). Statistical analyses were carried out using Statistica 8 software. Means and medians were calculated but other centiles were not (*potential weakness*). Pollen from *Brassica napus* in the pollen collected by bees during flowering of rape was large in most samples, up to 98% (Table 3).	
Use of GLP and QA/QC	Not a GLP study but a reasonably well described protocol but no QC.	**2**
Transparency of data	Raw data were not provided. Means and other summary data were provided in Tables.	**2**
Number of samples and replication	Over two years there were five sites and only a single field for each product. Samples in fields were pseudoreplicated.	**2**
Duration of study sufficient to observe trends	The duration of the study was sufficient for the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**2.6**
Score for expert judgment on Quality of the study.	**1**	**2.60**

Relevance

Hazard quotient for maximum concentration of TMX in pollen and nectar from OSR (Tables 6 and 7)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Nectar collected from flowers of wOSR treated with TMX	Mean conc. (n = 6)	0	0.00	8.6	Adult	292
Nectar collected from the hive of wOSR treated with TMX	Mean conc. (n = 10)	2.4	0.70	8.6	Adult	292
Honey collected from the hive of wOSR treated with TMX	Mean conc. (n = 10)	1.8	0.53	8.6	Adult	292

Hazard quotient for maximum concentration of TMX in pollen and nectar from OSR (Tables 6 and 7)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Pollen loads collected from the hive of wOSR treated with TMX	Mean conc. (n = 20)	0	0.00	8.6	Larva	124
Bee-bread collected from the hive of wOSR treated with TMX	Mean conc. (n = 10)	0	0.00	8.6	Larva	124
Nectar collected from flowers of sOSR treated with TMX	Mean conc. (n = 7)	5.4	1.58	8.6	Adult	292
Nectar collected from the hive of sOSR treated with TMX	Mean conc. (n = 20)	10.3	3.01	8.6	Adult	292
Honey collected from the hive of sOSR treated with TMX	Mean conc. (n = 10)	7.7	2.25	8.6	Adult	292
Pollen loads collected from the hive of sOSR treated with TMX	Mean conc. (n = 25)	6.6	0.82	8.6	Larva	124
Bee-bread collected from the hive of sOSR treated with TMX	Mean conc. (n = 10)	3.6	0.45	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected from flowers of wOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected from the hives exposed to wOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey collected from the hives exposed to wOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.	**0**

Response 3: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen loads collected from the hives exposed wOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in bee-bread collected from the hives exposed to wOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected from flowers of sOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 7: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected from the hives exposed to sOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 8: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey collected from the hives exposed to sOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 9: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen loads collected from the hives exposed sOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 10: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in bee-bread collected from the hives exposed to sOSR grown from seeds treated with TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 8, 2016
SEJ	Yes	May 29, 2016

(Stewart et al. 2014)
Paper: Stewart SD, Lorenz GM, Catchot AL, Gore J, Cook D, Skinner J, Mueller TC, Johnson DR, Zawislak J, Barber J. 2014. Potential exposure of pollinators to neonicotinoid insecticides from the use of insecticide seed treatments in the Mid-Southern United States. Environmental Science & Technology 48:9762-9769

This study was based on samples collected from small plot evaluations of seed treatments and from commercial fields in agricultural production areas in Arkansas, Mississippi, and Tennessee. Samples of soil, pollen, nectar, honeybees, and wildflowers were analyzed for concentrations of clothianidin, imidacloprid, and TMX and their metabolites. Unfortunately, bee-relevant nectar and pollen were not collected from the wildflowers but the whole flower was analyzed instead. These latter data are not usable in the WoE and only the data for TMX from pollen from corn and cotton were included in this WoE.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	This study was conducted in 2012. The general locations of the field sites were reported (Table S3) but the precise locations of the field sites were not. Plot length varied from 9.1 to 13.7 m and there were no foliar applications of neonicotinoid insecticide prior to sampling. How far they were from other fields was not reported. The corn variety was DeKalb DKC66-96. Seeds were treated with: no insecticide, TMX (0.25 and 0.5 a.s. mg/seed, as Cruiser 5F®). Concentrations in the seed were not verified by analysis (*potential weakness*) but soil samples did show the presence of residues (Table 3). Pollen from corn was collected by placing 25 tassels from each plot in a brown paper sack and transporting it to the laboratory. In the laboratory, tassels were beaten on the sides of an 18.9 L plastic bucket for several seconds. The pollen and anthers were then brushed into a sieve (6 mm; large mesh (*potential weakness*)) placed over a disposable paper plate. Sieving with the aid of a brush separated anthers and most other debris from the pollen. Pollen was then stored in microcentrifuge tubes. Corn pollen was composited by treatment across replicates within each of the four locations. Analyses of pollen from cotton were conducted as well and TMX was detected in only one sample (1.1 µg/kg). Because of lack of detail on collections and pooling of samples, these data are not included in the WoE. All samples collected in this study were transported either on coolant packs or dry ice to a laboratory for processing, after which they were stored at -4 to -15°C. Shipment of samples was done in ice chests containing dry ice or coolant packs. Samples were stored from 6 - 12 months before being analyzed but the storage temperature was not reported. Reported temperatures were >-18°C and transport and storage blanks were not reported (***major weakness***). Samples were analyzed at the USDA AMS Science and Technology Laboratory Approval and Testing Division of the National Science Laboratories' Gastonia Lab in Gastonia, NC. The samples were extracted using the QuEChERS method, and analyzed by LC/MS/MS). Quantification was performed using external calibration standards prepared from certified standard reference material of unreported purity (*potential weakness*). Internal isotopically-labelled standards were not reported used. The LODs for clothianidin, imidacloprid, and TMX were	**2**

Response 1: Quality of methods			Score
	1 µg/kg; LOQs were not reported (*weakness*). Percent recovery was not reported (*weakness*). TMX and clothianidin, were detected in pollen from untreated plots of corn and mean (±SE) concentrations of 0.1 ± 0.3 and 0.1 ± 0.25 µg/kg respectively (Table 2). TMX and clothianidin were detected in the soils of these plots (Table 3), which likely explains the detection of both residues in pollen. For this reason, concentrations of TMX and clothianidin were not combined. Statistical analysis was not conducted so medians and centiles were not available (*weakness*).		
Use of GLP and QA/QC	This study was not conducted under GLP and there was no QA or QC reported. A protocol was provided.		**1**
Transparency of data	Raw data were not provided. Only summary data were provided in Tables. It is not clear how many replicates there were. Percentages presented in Table 2 were not consistent with the number sites and pooling of replicates.		**1**
Number of samples and replication	For corn, there were four sites and four replicates (pooling of samples reduced the replicates to 1. For cotton, there were five sites but not all were sampled for nectar.		**2**
Duration of study sufficient to observe trends	It appears that only one sampling was undertaken during pollen shed and nectar secretion.		**1**
Overall evaluation of methods	Computed mean of above		**1.4**
Score for expert judgment on Quality of the study. The lack of appropriate storage and transport spikes, the lack of information on conditions of long-term storage, and the use of transport temperatures >-18°C are a ***major weakness***.		**0.5**	**0.70**

Relevance

Hazard quotients for mean concentration of TMX in pollen from corn grown from treated seed in the USA (Table 2 & p 9765)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Corn from seed treated with TMX at 0.25 mg/seed	Pollen from plants (mean)	0.4	0.05	8.6	Larva	126
Corn from seed treated with TMX at 0.5 mg/seed	Pollen from plants (mean)	0.4	0.05	8.6	Larva	126

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen of maize crops planted with seed treated with two different levels of TMX resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	April 8, 2016
SEJ	Yes	May 29, 2016

(Stoner and Eitzer 2012)
Paper: Stoner KA, Eitzer BD. 2012. Movement of soil-applied imidacloprid and thiamethoxam into nectar and pollen of squash (*Cucurbita pepo*). PLoS ONE 7:e39114. 6 p.

This was study of exposures to IMI and TMX applied to summer squash after application either to the seed hole just before planting (direct seeded) or to the transplanted plant through drip irrigation. Products were applied at rates within the recommended range. Analyses were conducted on whole plants, flowers, flower, parts, pollen and nectar. Only the latter two sets of data for TMX were assessed in this WoE. Treatments 2 and 4 were assessed in the WOE IMI.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted over two years (2009 and 2010) in two different fields, neither of which had been treated with TMX previously. In 2009, *Cucurbita pepo* L. cv. ‘‘Multipik,’’was grown on black plastic mulch in rows on 1.5 m centers with seed holes spaced at 0.9 m. For the direct-seeded treatments, three seeds were planted per hole. For the transplanted treatments, three seeds per cell were started in the greenhouse before transplanting, and one cell was transplanted per seed hole. Fertilizer was applied as recommended based on tests of soil. The field was laid out in a randomized complete block design with three blocks and five treatments (only three were relevant in this WoE): 1) Untreated control 3) TMX at 140 g a.s./ha (Platinum®, Syngenta Crop Protection) applied by surface spray to the soil in the planting hole and immediately incorporated into the soil with hand tools. 5) TMX at 140 g a.s./ha (Platinum®, Syngenta Crop Protection) applied using a Venturi injector through drip irrigation to the entire row five d after transplanting. In 2010, three blocks were planted with *Cucurbita pepo* L. cv ‘‘Sunray F1’’ and a fourth block was planted with winter squash, *Cucurbita pepo* L. cv. ‘‘Bush Delicata.’’ In 2010, treatments were applied as in 2009, but at different rates. TMX was applied at 143 g a.s./ha. Concentrations in the application solution and/or soil were not measured (potential weakness). Each plot consisted of 3 rows, and all samples were taken from the center row in order to avoid edge effects. Nectar was collected with an Eppendorf pipette from female flowers that had been enclosed the previous afternoon in a pollinating bag. Nectar collection continued if female flowers were available in order to get as much nectar as possible for analysis. The nectar from all three blocks was pooled in 2009, and nectar from the three blocks of summer squash was pooled in 2010 to have enough nectar for reliable chemical analysis. Nectar from the winter squash in 2010 was collected later and analyzed separately. After collection, all samples (except for male flowers for pollen analysis) were kept in a cooler on an ice pack during the day of collection and then stored at -18°C until analysis. Pollen was hand-collecting from open male flowers that had been enclosed in a pollinating bag (as above). Flowers were collected from 6 until 10 am into a large plastic bag, which was then taken back to the laboratory where pollen was scraped by hand, using a thin plastic sheet, from the synandrium of each flower. The plastic bags of flowers	**2**

Responses 1-2: Quality of methods		Score
	were stored for up to one week at 4°C. In 2009, the pollen was pooled across all three blocks to have enough for analysis, but a second sample was taken a week later, also pooled across blocks. In 2010, enough pollen was collected to allow for separate block analyses. Controls (field blanks) were used. Analysis was well described in the paper but there was no internal standard reported used for the analysis of TMX (weakness). All samples were extracted using a modified version of the QuEChERS with analysis via LC/MS/MS. Based on spiked control samples, recovery averaged 95±18% LODs ranging from 0.5 to 2 µg/L depending on matrix and the amount of sample available. LOQs were not reported but the minimum concentration reported was 3-x the LOD. Statistical analysis was conducted with SYSTAT 2009 but this was not done for nectar because of sample pooling.	
Use of GLP and QA/QC	This was not a GLP study but the protocol was fully described and there was limited QC	**2**
Transparency of data	Raw data were not provided only means maxima and minima.	**2**
Number of samples and replication	Pooling of samples of pollen and nectar reduced replication; Although two sites were used across two years and there were subplots the data were combined across sites and years for presentation. However, the authors report 12 replicates for pollen and 6 for nectar.	**2**
Duration of study sufficient to observe trends	Duration of sampling of pollen was 1 week in 2009 and 2 weeks in 2010. For nectar, it was 1 week in 2009 and 2.5 weeks in 2010.	**3**
Overall evaluation of methods	Computed mean of above	**2.20**
Score for expert judgment on Quality of the study.	**1**	**2.20**

Relevance

Hazard quotients for exposures to TMX in honey bees via pollen and nectar from squash (data from Table 3).

Source	Matrix	Conc. TMX µg/kg	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg of food or water/d
Squash	Pollen min. (n = 12)	5	0.62	8.6	Larva	124
Squash	Pollen mean (n = 12)	12	1.49	8.6	Larva	124
Squash	Pollen max. (n = 12)	35	4.34	8.6	Larva	124
Squash	Nectar min. (n = 6)	5	1.46	8.6	Adult	292
Squash	Nectar mean (n = 6)	11	3.21	8.6	Adult	292
Squash	Nectar max. (n = 6)	20	5.84	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentrations of TMX measured in pollen collected from flowers of squash treated with TMX at the transplant stage resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The maximum concentrations of TMX measured in nectar collected from flowers of squash treated with TMX at the transplant stage resulted in exposures that were less than the NOAED for bees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

The major pollinators of squash in the eastern US where the study was conducted are squash bees, *Peponapis pruinosa*, a specialist pollinator feeding its larvae exclusively on pollen from the genus *Cucurbita*, bumble bees (*Bombus impatiens*), and honey bees.

Expert judgment		
QA	Yes	April 9, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2000a)
Report: Syngenta. 2000. Report on Analytical Study 100/99 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Honey and Sun Flower Heads Collected in Study 983769. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1363 - A9567B. 4 p

This report described the analysis of samples of flower-heads and honey from sunflowers exposed via seed-dressing with TMX[12]. The effects on bees are described in another WoE[13]. Imidacloprid was included as a reference compound but these data are not included in this WoE.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	This was a tunnel-study conducted in Merainville, central France (Beauce area). This test was conducted in tunnels erected over sunflowers grown from seeds treated with TMX at a rate of 350 g and 700 g a.s./100 kg seed. There was one control (untreated seed). The content of a.s on the seeds was not reported as confirmed by analysis, and neither was the formulation used to treat the seeds (*weakness*). The seeds (var. Cadasol) and were sown with pneumatic equipment on 1998-06-08. All plots were irrigated on 1998-06-13. The tunnels were 136.5 m^2 and were divided into four sub-plots, two of which were untreated refuges and two were treated (*weakness* as the exposures were reduced by an uncertain amount). Honeybees (*Apis mellifera mellifera*) were healthy and were from a local commercial source. Each hive contained approximately 10,000 bees. The hives were placed in the tunnels between 1998-08-12 and 1998-08-14 at flowering stage BBCH 61. Honey was sampled from the combs on 1998-08-26. A minimum of 50 mL was collected and held at -18C. Field blanks, spikes and transport spikes were not reported used (*weakness*). Samples of honey were diluted with pure water and then analyzed by LC MS/MS. Isotopically labeled internal standards were not used but standards of unstated purity were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX and clothianidin from honey ranged from 84–74% and 67–58% respectively. TMX was detected in flowers of the treated plants, but Clothianidin was not. TMX and Clothianidin were not detected in honey from treatment plots. Neither TMX nor Clothianidin were detected in flowers or honey from the control treatment.	**1**
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	One tunnel was used per treatment concentration and the study was conducted at one site only.	**1**

[12] Syngenta. 1998. Tunnel Test: Effects of Sunflowers Grown from Seeds Dressed with A-9567B on Honey Bees (*Apis mellifera*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_0957 - A9567B (S98NCR3769V074). 40 p
[13] Syngenta. 2000. Tunnel Test- Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 70 WS (A-9567 B) on Honey Bees (*Apis mellifera*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1408 - A9567B (S99NCB1556VO46). 123 p

Response 1: Quality of methods			Score
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.		**4**
Overall evaluation of methods	Computed mean of above		**2.8**
Score for expert judgment on Quality of the study.		**1**	**2.80**

Relevance

Hazard quotients for concentrations of TMX in honey produced by bees (data from p. 3).

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to sunflowers grown from treated seeds.	Honey (n = 2)	0	0.0	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 17, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2000f)
Report: Syngenta. 2000. Report on Analytical Study 104/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Leafs), Honey, Pollen, and Bee (Honey Stomach Content) Collected in Study 99332/S1-BFEU. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1367 - A9567B. 7 p

This report described the analysis of samples of flower-heads, leaves, honey, pollen and nectar collected by bees from sunflowers exposed via seed-dressing with TMX[14]. The effects on bees are described in the WoE for effects. Imidacloprid (Gaucho 70 WS) was included as a reference compound but these data are not included in this WoE.

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	This was a field-study conducted in the south west of Spain near 02640 Almansa. The fields were 4 ha in area and were 6 km apart. No imidacloprid had been used in the "last few years". Sunflower seeds (var. Sambro) were treated with CGA 293343 WS 70 (A 9567 B) at a measured rate of 369 g TMX/100 kg seed. There was one control. All seeds were treated with Quinolate Pro FL (0.25 L/100 kg seeds; 12 % (w/v) oxine copper and 12 % (w/v) carbendazim), a fungicide. Seeds were sown with pneumatic equipment on 1999-05-15 at a rate of 7.5 kg seed/ha. Meteorological conditions were recorded during the study. Six hives in two groups were located on each treatment field (test, control, and reference treatment). Honeybees (*Apis mellifera mellifera*) were from a local commercial source and certified as healthy. Each colony contained 1 body with 12 frames including frames with brood and frames with pollen and/or nectar. Number of bees per hive was not stated. The hives were placed in the fields when the sunflowers were at BBCH-stage: 61-62, start of blooming. After flowering (17th of August) all bee hives were transported to a forest area (La Casa Navarro). Honey was sampled by removal of one comb on 1999-08-02, 1999-08-11, and 1999-09-09, each from a different hive. An empty comb was used to replace the sampled comb. The comb was frozen at -20C. Pollen collected by forager bees was removed in a pollen trap. Hives were sampled in sequence for at least 24 h. Samples were collected daily from 1999-07-26 to 1999-08-01. The origin of the pollen was determined. Collected samples were stored at -20C. Nectar was collected from the honey stomach. Forager bees (ca. 200 per sample) were collected four times per colony with a CO_2 gun and were stored at -20C and shipped at the same temperature to the Niedersächsisches Landesinstitut für Bienenkunde for removal of the nectar from the honey stomach. The bees were thawed and the honey-stomach removed and examined for the presence of pollen under a microscope. The honey stomach contents of the same origin (same pollen indicated the same nectar source), colony, and sampling date were pooled for analysis. The samples were again frozen at -20C and shipped frozen	**3**

[14] Syngenta. 2001. Field Test: Side Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 WS 70 (A 9567 B) on the Honey Bee (*Apis mellifera* L.) in Spain. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1361 - A9567B (99332/S1-BFEU). 104 p

Responses 1-3: Quality of methods		Score
	for analysis. Plant samples were collected but are not discussed here other that they contained residues of TMX and clothianidin. Field control samples were analyzed; spikes and transport spikes were not reported used (*weakness*). Samples of honey in the comb were allowed to flow into a beaker held at 40°C for 4 hours. Honey and nectar were diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of unstated purity were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey, nectar and pollen ranged from 76–79%, 86–92% and 91–116%, respectively. Recovery for clothianidin was 79–85%, 87–87% and 56–71%, respectively. Clothianidin was not detected in honey, pollen, or nectar. Neither TMX nor clothianidin were detected in control samples of honey, pollen, or nectar.	
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was only one site per treatment but there were 6 pseudoreplicated hives per site, which were sampled in groups of 3.	**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.	**4**
Overall evaluation of methods	Computed mean of above	**3.2**
Score for expert judgment on Quality of the study.	**1**	**3.20**

Relevance

Hazard quotients for concentrations of TMX in pollen, nectar and honey produced by bees (data from p 5).

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to sunflowers grown from treated seeds.	max. in honey (n = 11)	1	0.3	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in nectar (n = 5)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in pollen (n = 7)	1.1	0.14	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.	**0**

Response 1: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 17, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2000e)
Report: Syngenta. 2000. Report on Analytical Study 106/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Flowers), Honey, Nectar, and Pollen Collected in Study 31061/00. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1364 - A9567B. 5 p

This report described the analysis of samples of flower-heads, leaves, honey, pollen and nectar collected by bees from sunflowers exposed via seed-dressing with TMX[15]. The effects on bees are described in the WoE for effects. Imidacloprid (Gaucho 600 FS) was included as a reference compound but these data are not included in this WoE.

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	This was a field-study conducted in Hungary. The treated fields were 4.5-4.2 ha in area and were 2 km apart. Two control fields (4.5 and 16 ha were used). No imidacloprid had been used in the fields previously. Sunflower seeds (var. Alexandra) were treated with CGA 293343 350 FS (A-9700 B) a measured rate of 351 g a.s./L (Section 3.1.1). The nominal application rate to seeds was reported (Section 3.4.1) as 42g a.s./150,000 seeds. All seeds were treated with fungicide (metalaxyl, mancozeb, and benomyl; Table 5). The reference field was treated with imidacloprid (Gaucho 600 FS). The fields were treated post-plant with herbicides (acetochlor, dichlorrnid, fluorchloridon, prometrin, S-metolachlor, oxyfluorfen, and dimethenamid following good agricultural practice; Table 3). Seeds were sown with an SPC-6 seeder on 2000-04-12 at a rate of 66,667 seeds/ha. For Control field II, seeds were sown with a IHC-Cyclo-400 on 2000-04-18 at a rate of 53,000 seeds/ha. Meteorological conditions were recorded during the study (Appendix 16). Sixty hives were used in the study, fifteen in each of the test, two controls, and reference treatment. Honeybees (*Apis mellifera carnica*) were from a local commercial source and certified as healthy. Each hive contained 30 combs. Number of bees per hive was not stated. The hives were placed in the fields when the sunflowers were at BBCH-stage: 61-62, start of blooming (2000-06-22). After flowering (2000-07-05) all bee hives were transported back to the source apiary. Sampling took place between 2000-06-30 and 2000-07-05 (Table 6); 100 g fresh honey was taken from each of two hives, 10 ml fresh nectar from each of two hives and pollen was collected in pollen traps from two hives on two different days. The samples were frozen at -20C. The origin of the pollen was not determined (*potential weakness*). Samples of flower heads were taken for analysis and contained detectable residues of TMX only. Field control samples were analyzed; spikes and transport spikes were not reported used (*weakness*). Honey and nectar were diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC	**3**

[15] Syngenta. 2001. Field test: Side Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 350 FS (A-9700 B) on the Honeybee (*Apis mellifera carnica*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1369 - A9700B (31061/00). 99 p

Responses 1-3: Quality of methods			Score
	MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey, nectar and pollen ranged from 88–93%, 82–90%, and 69–85% respectively. Recovery for clothianidin was 95–105%, 89–94% and 68–76% respectively Neither TMX nor clothianidin were detected in control samples of honey, pollen, or nectar.		
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA.		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was only one site per treatment but there were 15 pseudoreplicated hives per site, only two of which were sampled.		**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.		**4**
Overall evaluation of methods	Computed mean of above		**3.2**
Score for expert judgment on Quality of the study.		**1**	**3.20**

Relevance

Hazard quotients for concentrations of TMX in pollen, nectar and honey produced by bees (data from p 4)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to sunflowers grown from treated seeds.	max. in honey (n = 2)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in nectar (n = 2)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in pollen (n = 4)	0	0.0	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.	**0**

Response 2: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 17, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2000c)
Report: Syngenta. 2000. Report on Analytical Study 107/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Flowers), Honey, Nectar, and Pollen Collected in Study 31062/00. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1365 - A9567B. 5 p

This report described the analysis of samples of flower-heads, leaves, honey, pollen and nectar collected by bees from sunflowers exposed via seed-dressing with TMX[16]. The effects on bees are described in another WoE based on Report CGA293343-1370[10].

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	This was a field-study conducted in Tolna in Hungary. The treated field was 63.2 ha and control was 155 ha in area and the fields were 8 km apart. No imidacloprid had been used in the fields previously. Sunflower seeds (var. Alexandra) were treated with CGA 293343 350 FS (A-9700 B) a measured rate of 351 g a.s./L (Section 3.1). Application rate on seeds was 0.12 L/150,000 seeds which was nominally equivalent to 42 g a.s./150,000 seeds. Seeds were also treated the fungicides metalaxyl, mancozeb, and benomyl. The fields were treated post-plant with herbicides (prometrin, oxyfluorfen, and dimethenamid) and fungicides (flusilazole, carbendazim, and vinclozolin) following good agricultural practice; Table 3). Seeds were sown with an IHC-Cyclo-400 seeder on 2000-04-12 (treatment field) and 2000-04-11 to 13 (control field) at a rate of 63,200 seeds/ha (17.696 g a.s./ha). Meteorological conditions were recorded during the study (Table 16). Thirty hives were used in the study, fifteen in each of the test and control. Honeybees (*Apis mellifera carnica*) were from a local commercial source and certified as healthy. Each hive contained 30 combs. Number of bees per hive was not stated. The hives were placed in the fields when the sunflowers were at the start of blooming (2000-06-22). After flowering (day 12 of the experiment; 2000-07-04), all bee hives were transported back to the source apiary. Sampling took place between 2000-06-30 and 2000-07-04; 100 g fresh honey was taken from each of two hives, 10 ml fresh nectar from each of two hives and pollen was collected in pollen traps from two hives on two different days. The samples were frozen at -20C. The origin of the pollen was not determined (*potential weakness*). Samples of flower heads were taken for analysis and contained detectable residues of TMX only. Field control samples were analyzed; spikes and transport spikes were not reported used (*weakness*). Honey and nectar were diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods.	**3**

[16] Syngenta. 2001. Field test: Side Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 350 FS (A-9700 B) on the Honeybee (*Apis mellifera carnica*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1370 - A9700B (31062/00). 77 p

Responses 1-3: Quality of methods			Score
	Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey, nectar and pollen ranged from 88–93%, 82–90%, and 69–85% respectively. Recovery for clothianidin was 95–105%, 89–94% and 67–76% respectively. Clothianidin was not detected in the pollen, honey, nectar, or in the sunflower heads. Neither TMX nor clothianidin were detected in control samples of honey, pollen, or nectar.		
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA.		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was only one site per treatment but there were 15 pseudoreplicated hives per site, only two of which were sampled.		**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.		**4**
Overall evaluation of methods	Computed mean of above		**3.2**
Score for expert judgment on Quality of the study.		**1**	**3.20**

Relevance

Hazard quotients for concentrations of TMX in pollen, nectar and honey produced by bees (data from p 4)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to sunflowers grown from treated seeds.	max. in honey (n = 2)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in nectar (n = 3)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in pollen (n = 4)	0	0.0	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.	**0**

Response 2: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 18, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2001b)
Report: Syngenta. 2001. Report on Analytical Study 103/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sunflowers (Flowers, Leaves), Honey, Honey Stomach Content, and Pollen, Collected in Study 20001072/I1-BFEU. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1411- A9567B. 5 p

This report described the analysis of samples of flower-heads, leaves, honey, pollen and nectar collected by bees from sunflowers exposed via seed-dressing with TMX[17]. Imidacloprid was used as a reference but is not discussed in this WoE. The effects on bees are described in the WoE for effects based on Report CGA293343-1391[11].

Responses 1-2: Quality of methods		Score
Experimental design and hypotheses	This was a field-study conducted near Bologna in Italy. There were three fields, a TMX treatment, a control, and a reference. All fields were approximately 2 ha in size and the test item to control and reference fields were ~20 km apart, however the reference and control fields were only 4 km apart. No imidacloprid had been used in the fields in the last few years. Sunflower seeds (var. Carlos) were treated with CGA 293343 Cruiser® 70 WS (A-9567 B). Application rate on seeds was measured at 339.9 g a.s./100 kg seeds. All seeds were treated with a fungicide (Apron XL 350 ES; 200 g a.s. (metataxyl-M)/100 kg seeds)) and no other pesticides were reported used on the sunflowers during growth. A reference field was treated with imidacloprid (Gaucho 70 WS). Seeds were sown with an Agricola Italiana Massanzago PD pneumatic seeder on 2000-04-17 at a rate of 88,949 seeds/ha for the test item field and 97,544 seeds/ha for the control field. Meteorological conditions were recorded during the study and combined with data from local weather stations (Tables 11 - 16). Eighteen hives were used in the study, six in each of the test, reference, and control fields. Honeybees (*Apis mellifera ligustica*) were from a local commercial source and certified as healthy. Each hive contained 1 brood body with at least 5–9 brood frames and 1–2 honey body with 8–10 frames. Number of bees per hive was 25,000–35,000. The hives were placed in the fields when the sunflowers were at BBCH-stage: 59-62, start of blooming (2000-06-21) in two groups of 3. After flowering (2000-07-01) all bee hives were transported another location. Sampling of honey took place on 2000-08-08 from the group-1 hives and during the hive appraisals for group-2 (2000-06-23 and 2000-06-30). Honey was extracted from the comb with a honey extractor or the entire honey comb was removed and placed into a plastic bag. All samples were stored at -18C. Pollen traps were used to collect pollen from returning foragers. Nectar was collected from the honey stomach. Forager bees were collected four times per colony with a CO_2 gun and were stored at -18C and shipped at the same temperature to the Niedersächsisches Landesinstitut für Bienenkunde for removal of the	**2**

[17] Syngenta. 2001. Field Test: Side Effects of Sunflower Grown from Seeds Dressed with A-9567 B on the Honey Bee (*Apis mellifera* L.) in Italy. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1391 - A9567B (20001072/I1-BFEU). 94 p

Responses 1-2: Quality of methods			Score
	nectar from the honey stomach. The bees were thawed and the honey-stomach removed and examined from the presence of pollen under a microscope. The honey stomach contents of the same origin (same pollen indicated the same nectar source), colony, and sampling date were pooled for analysis. The samples were frozen at -18C. Although the nectar samples were collected, they were not reported analyzed (*weakness*). Samples of flower heads and leaves were taken for analysis and only leaves contained detectable residues of TMX only. Field control samples were analyzed; spikes and transport spikes were not reported used (*weakness*). Honey was diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey and pollen ranged from 95–102% and 83-84% respectively. Recovery for clothianidin was 101–110% and 78–87% respectively. TMX was detected in pollen collected from the control hives (1.1 µg/kg) (***major weakness***).		
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA. Weather data were not recorded under GLP.		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was only one site per treatment but there were six pseudoreplicated hives per site, which were sampled in groups of three.		**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.		**4**
Overall evaluation of methods	Computed mean of above		**3**
Score for expert judgment on Quality of the study. The presence of TMX in pollen from the control plots was identified as a major weakness.		**0.5**	**1.50**

Relevance

Hazard quotients for concentrations of TMX in honey and pollen produced by bees (data from p 4)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to sunflowers grown from treated seeds.	max. in honey (n = 6)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in pollen collected by bees and from flowers (n = 3)	3.2	0.4	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 18, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2001c)
Report: Syngenta. 2001. Report on Analytical Study 102/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Winter Rape (Leaves, Blossoms), Honey, Honey Stomach Content, and Pollen, Collected in Study 99393/01-BFEU. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1830. 6 p

This report described the analysis of samples of blossoms, leaves, honey, pollen and nectar collected by bees from oil-seed winter-rape (wOSR) exposed via seed-dressing with TMX[18]. The effects on bees are described in WoE_{Eff} based on Report CGA173506-5423[12].

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	This was a field-study conducted Germany near Pforzheim. There were two fields, a treatment (3.9 ha) and a control (4.3 ha), which were 3 km apart. Winter oil-seed rape seeds (*Brassica napus* var. Express) were treated with Cruiser® OSR also containing the fungicides metalaxyl-M and fludioxonil. Application rate on seeds was measured at 416 g TMX/100 kg seeds. The report indicated that no other plant protection products were used on the wOSR during growth but the history of use of neonicotinoids was not provided (*weakness*). Seeds in the treated and control fields were sown with a pneumatic seeding machine by Accord and Amazone at 4.2 kg and 4.01 kg /ha, respectively. Dates of sowing were 1999-08-19 and 1999-08-30, respectively. A reference chemical was not used. Meteorological conditions were recorded during the study and combined with data from local weather stations (Tables 9 - 11). Eighteen hives were used in the study, six in each of the test, reference, and control fields. Honeybees (*Apis mellifera carnica*) were from a local commercial source and certified as healthy. Each colony contained 2-3 brood bodies with at least 8 brood frames and at least 19 honey frames. The number of worker bees ranged from 30,000–40,000 per colony. The hives were placed in the fields when the OSR were at BBCH-code: 59–60, start of blooming (2000-04-20) in two groups of 3. After flowering (2000-05-10) all bee hives were transported another location (Königsbach-Stein). Sampling of honey took place from the group-2 hives during the hive appraisals (2000-04-25, 2000-05-02, and 2000-05-10). An entire comb was removed and frozen at -18C. The method of collection of pollen was not clear. It is stated that a pollen trap could not be used on the test hives but one was apparently fixed to the front of hive-5 for one day. Pollen traps were used to collect pollen from returning foragers. Nectar was collected from the honey stomach. Forager bees were collected four times per colony with a CO_2 gun and were stored at -18C and shipped at the same temperature to the Niedersächsisches Landesinstitut für Bienenkunde for removal of the nectar from the honey stomach. The bees were thawed and the honey-stomach removed and examined from the presence of pollen under a	**2**

[18] Syngenta. 2001. Field Test: Side Effects of Oil-Seed Winter-Rape Grown from Seeds Dressed with Cruiser OSR (A9807 C) on the Honey Bee (*Apis mellifera* L.). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA173506_5423 - A9807C (99393/01-BFEU). 80 p

Responses 1-3: Quality of methods			Score
	microscope. The honey stomach contents of the same origin (same pollen indicated the same nectar source), colony, and sampling date were pooled for analysis. The samples were frozen at -18C. Samples of flowers and leaves were taken for analysis and contained detectable residues of TMX. Samples of leaves also contained detectable residues of clothianidin. Field control samples were analyzed; spikes and transport spikes were not reported used (*weakness*). Honey and nectar were diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey, nectar, and pollen ranged from 91–112%, 97–102 and 59–64%, respectively. Recovery for clothianidin was 100–111%, 91–96%, and 72–80%, respectively. TMX was detected in nectar collected from the control bees (1.0 µg/kg) (***major weakness***). Clothianidin was detected in nectar collected from the bees from the TMX-treated wOSR field (1.0 µg/kg).		
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA. Weather data were not recorded under GLP.		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was only one site per treatment but there were six pseudoreplicated hives per site, which were sampled in groups of three.		**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.		**4**
Overall evaluation of methods	Computed mean of above		**3**
Score for expert judgment on Quality of the study. The presence of TMX in nectar from bees in the control plot was identified as a major weakness.		**0.5**	**1.50**

Relevance

Hazard quotients for concentrations of TMX in honey, nectar, and pollen produced by bees (data from p 4-5)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to OSR grown from treated seeds.	max. in honey (n = 18)	0.0	0.0	8.6	Adult	292
Hives exposed to OSR grown from treated seeds.	max. in nectar from bees (n = 5)	1.2	0.34	8.6	Adult	292
Hives exposed to OSR grown from treated seeds.	max. in pollen collected by bees from flowers (n = 1)	0.0	0.0	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via OSR grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from forager bees exposed to TMX via OSR grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via OSR grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 18, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2001d)
Report: Syngenta. 2001. Report on Analytical Study 112/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Oil Seed Rape (Flowers), Honey, Honey Stomach Content, and Pollen, Collected in Study 00 10 48 016. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1832. 6 p

This report described the analysis of samples of flowers, honey, pollen and nectar collected by bees from oilseed rape exposed via seed-dressing with TMX[19]. The effects on bees are described in another WoE based on Report CGA172506-5395[13].

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	This was a field-study conducted Germany near Leipzig (Sachsen). There were two fields, a treatment (1.59 ha) and a control (1.14 ha) and were 5 km apart. Seeds of spring oil-seed rape (*Brassica napus* var. Forte) were treated with A-9807 C also containing the fungicides metalaxyl-M and fludioxonil. Application rate on seeds was measured at 401.2 g TMX/100 kg seeds. No other pesticides were used on the sOSR after sowing until the end of flowering and removal of bees from the trial but the history of use of neonicotinoids was not provided (*weakness*). Seeds in the treated and control fields were sown with a pneumatic seeding machine by pneumatic seed drill Accord + electronic sowing control at 8 kg seeds/ha. Date of sowing was 2000-04-10. A reference chemical was not used. Meteorological conditions were recorded during the study and combined with data from local weather stations (Appendix 2). Twelve hives were used in the study, six in each of the test and control. Honeybees (*Apis mellifera*) were from a local commercial source and were healthy. Each colony contained 11 frames with 6-10 frames occupied with brood in the different stages; 1 honey and pollen super: 11 frames including 10 constructed honey combs and 1 foundation were provided to give enough space for bees, honey and pollen. The number of worker bees ranged from 60,000-80,000 per colony. The hives were placed in the fields when the sOSR were at BBCH-code: 61 (2000-06-05/06 for treatment and control, respectively). Sampling of took place from BBCH 64 (2000-06-10) to BBCH 67 2000-06-26). The sampling of pollen, flowers, soil, honey, and live bees was described in Section 2.4.5 and in a summary Table in Appendix 4. How the samples were stored was not reported but it is stated that the samples arrived for analysis frozen at -18C. The preparation of the nectar samples (non-GLP) was described in the analytical report. Bees of one sample were thawed for a few minutes, were fixed with a needle through the thorax and their abdomens were gently stretched with a pair of forceps. The abdomens or the tergite plates were removed, so that the honey stomachs were free. The honey stomach was held at the very end of the esophagus, which was removed and was transferred onto a tarred slide for observation under a light microscope.	**2**

[19] Syngenta. 2001. Assessment of Side Effects of CGA 293343 + CGA 329351 + CGA 173506 FS 321.3 (A 9807 C) Applied as Seed Dressing of *Brassica napus* on the Honeybee *Apis mellifera* L. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA173506_5395 - A9807C (2003626). 59 p

Responses 1-3: Quality of methods		Score
	The contents of the honey stomachs were pooled for the same treatment and sampling date and stored at approximately- 18C for subsequent analysis. Field control samples were analyzed; spikes and transport spikes were not reported used (*weakness*). Samples of honey in the comb were allowed to flow into a beaker held at 50C for 2 h. Honey and nectar were diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey and pollen ranged from 86-95% and 59–64%, respectively. Recovery of clothianidin was 98–110% and 72–80, respectively. TMX was detected in the rape flowers. No residues were detected in the controls.	
Use of GLP and QA/QC	The effects component and the analysis of residues were conducted under GLP with QA. Weather data were not recorded under GLP. Collection of the nectar from the forager bees was in the spirit of GLP	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was only one site per treatment but there were six pseudoreplicated hives per site.	**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.	**4**
Overall evaluation of methods	Computed mean of above	**3**
Score for expert judgment on Quality of the study.	**1**	**3.00**

Relevance

Hazard quotients for concentrations of ΣTMX in honey, nectar, and pollen produced by bees (data from p 4)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to OSR grown from treated seeds.	max. in honey (n = 1)	0	0.0	8.6	Adult	292
Hives exposed to OSR grown from treated seeds.	max. in nectar from bees (n = 1)	0	0.0	8.6	Adult	292
Hives exposed to OSR grown from treated seeds.	max. in pollen collected by bees (n = 5)	4.8	0.6	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the above Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via OSR grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from forager bees exposed to TMX via OSR grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via OSR grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 19, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2002)
Report: Syngenta. 2002. Determination of Residues of Thiamethoxam (CGA 293343) and CGA 322704 in Maize Plants and Maize Pollen after Seed Dressing with A9567C. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_1643. 17 p

The objective of this study was to determine the concentration of residues of TMX and its metabolite clothianidin in maize (whole plants and pollen) grown from treated seed. Only the values for pollen are discussed in this WoE.

Response 1: Quality of methods			**Score**
Experimental design and hypotheses	This study was conducted in in Ivenrode, Germany. The formulation code was A9567C WS 70. The treatment and control plots were 60 m^2 and were planted on 2000-04-26. The seeds were *Zea mays* var. Bahia and the measured application rate was 285.3 g a.s./100 kg seed. History of use of neonicotinoids in the field was not reported. The herbicides Gardoprim Plus (metolachlor) and Motivell (nicosulfuron) were applied to the maize following normal agricultural practices. Sampling took place during flowering, between 2000-07-17 and 2000-07-28. Weather data were collected (non-GLP). Pollen was collected from the anthers by an unspecified method (*weakness*). Immediately after sampling, the material was packed into polyethylene bags, labelled and deep frozen on the same day. The specimens were stored at ca. -18C. All specimens were transported in deep frozen conditions to Syngenta AG, Residue Analysis, Basel. Control samples were taken. Storage and transport spikes were not reported. Analysis followed a standard method (REM 179.03) and was by HPLC-MS/MS. The LOQ for TMX and clothianidin was 1 µg/kg and the recovery was 93-111% and 93-95% respectively in pollen. TMX and clothianidin were not detected in the controls		**2**
Use of GLP and QA/QC	The study was conducted under GLP (except for the weather data)		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was one site and one replicate. Analyses were in duplicate (pseudoreplicated).		**1**
Duration of study sufficient to observe trends	The duration of the study was appropriate to the objectives.		**4**
Overall evaluation of methods	Computed mean of above		**3**
Score for expert judgment on Quality of the study.		**1**	**3.00**

Relevance

Hazard quotients for concentrations of ΣTMX in pollen from maize plants (data from p 3)

Source of matrix	**Sample**	**Conc. ΣTXM in µg/kg or L**	**Dose ng/bee**	**Chronic NOAED ng/bee/d**	**Life-stage**	**mg diet/d**
Maize plants grown from seed treated with TMX	max. in pollen	6.5	0.8	8.6	Larva	124

Hazard quotients for concentrations of ΣTMX in pollen from maize plants (data from p 3)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
	collected by bees (n = 1)					

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected directly from maize plants resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 19, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2003a)
Report: Syngenta. 2003. Determination of Analytes Thiamethoxam (CGA 293343) and Its Metabolite CGA 322704 in or on Pollen, Nectar and Honey from Sunflower Collected in Study 991567. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1704. 10 p

This report described the analysis of samples of honey, pollen and nectar collected by bees from sunflowers exposed via seed-dressing with TMX[20]. A reference field was treated with imidacloprid (Gaucho 60 FS); these data are not included in the WoE. The effects on bees are described in the WoE_{EFF} based on Report CGA293343-1697[14].

Response 1-3: Quality of methods		Score
Experimental design and hypotheses	This was a field-study conducted in Argentina. The treated field was 2.1 ha and control was 2.2 ha in area. The reference field was 2.04 ha and the fields were ≥4 km apart. No imidacloprid has been used in the fields in the previous few years. Sunflower seeds (var. Paraiso 20 G2,) were treated with CGA 293343 350 FS (A-9700 B) at a nominal rate of 210 g a.s./100 kg seed (Section 7.2). Application rate on seeds was measured. Seeds were not treated any fungicides. Reference seeds were treated with imidacloprid (Gaucho 60 FS). Seeds were sown with a Migra with 5-unit seeder on 2000-12-28 at a rate of 56,584 seeds/ha. Meteorological conditions were recorded during the study (Table 13 and 14 in Appendix 1). Eighteen hives were used in the study, six in each of the test, the reference and the control fields. Honeybees (*Apis mellifera*) were from a local commercial source and certified for health. Each hive contained Each colony contained a brood body with 6-8 brood frames and one honey body with at least 8 frames. Number of bees per hive was not stated. The hives were placed in the fields in two groups of three per field when the sunflowers were at BBCH-stage: 61-62, start of blooming (2001-02-21). After flowering (2001-03-02) all bee hives were transported back to the source apiary (2001-03-06). Sampling took place between 2001-02-23 and 2001-03-06; fresh honey and nectar was taken from two different hives and pollen was collected in pollen traps. The pollen trap was attached during the main period of flowering, on at least three days (one day per hive) and for at least three hours per day. Pollen was also collected directly from the flower heads in plastic bags. Forager bees were captured at the entrance of the hive and frozen and then shipped frozen to Ecological Sciences, Syngenta Crop Protection AG Freshly collected nectar was collected from the honey stomach after the bees were thawed. Bees were fixed with a needle at their thorax and their abdomens were gently stretched with a pair of forceps. The abdomens or the tergite plates were removed so that the honey stomachs were freed and the front part of the esophagus was removed. The stomach was squeezed with the forceps and the extruding honey collected in a glass vial and then	**2**

[20] Syngenta. 2003. Field Test: Side Effects of Sunflower Grown from Seeds Dressed with A-9700 B on Honey Bee (*Apis mellifera* L.) in Argentina. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1697 - A9700B (991567). 52 p

Response 1-3: Quality of methods			Score
	frozen. The samples were frozen at -20C until analysis. The origin of the pollen was not determined (*potential weakness*). Field control samples were analyzed; field spikes and transport spikes were not reported used (*weakness*). Honey and nectar were diluted with pure water, cleaned up in an EN cartridge and then analyzed by LC MS/MS. Pollen was extracted in acetonitrile, cleaned up and then analyzed by LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey and pollen ranged from 86–113% and 69–88% respectively. Recovery for clothianidin was 78–86% and 62–76% respectively. TMX was detected in the pollen collected from the flowers in the control but not in the treated plants (1.3 and 4.4 µg/kg). This might have been a labelling mix-up but was identified as a (***major weakness***).		
Use of GLP and QA/QC	The study was not conducted under GLP but a full protocol and QC was provided.		**2**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was only one site per treatment but there were 6 pseudoreplicated hives per site, only one or two of which were sampled.		**1**
Duration of study sufficient to observe trends	Duration of the study was appropriate to the design.		**4**
Overall evaluation of methods	Computed mean of above		**2.6**
Score for expert judgment on Quality of the study. Presence of TMX in the pollen collected from the flowers of the control plot was identified as a ***major weakness***.		**0.5**	**1.30**

Relevance

Hazard quotients for concentrations of TMX in pollen, nectar and honey produced by bees (data from p 4-5)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Hives exposed to sunflowers grown from treated seeds.	max. in honey (n = 1)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in nectar from hive (n = 1)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in nectar from bees (n = 4)	0	0.0	8.6	Adult	292
Hives exposed to sunflowers grown from treated seeds.	max. in pollen collected by bees and from flowers (n = 4)	0	0.0	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from hives exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 19, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007b)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A Residue Study with A9700B Treated Spring Barley Seed Followed by A9807C Treated Winter Oil-Seed Rape Seed, Investigating Residues in Crop and Honeybee Products in Northern France. Bracknell Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10673 A9807C. 145 p

The objective of the semi-field (tunnels) study was to determine the concentration of TMX and its metabolite clothianidin in crop and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for spring barley followed by winter oilseed rape (wOSR).

Responses 1-7: Quality of methods		**Score**
Experimental design and hypotheses	The methods used in this study were well described. The site was Marest-Dampcourt, Picardie in Northern France and the study was conducted in 2005-2006. Seeds of spring barley (var. Seco), treated with CGA293343 FS (350) A9700B (analyzed at 354 g TMX/L and 720 g TMX/100 kg seed) were sown on 2005-03-17. Spring barley control seeds were untreated. The wOSR seeds (var. Roxet), treated with CGA173506/ CGA293343/ CGA329351 FS (A9807C) containing TMX, fludioxonil, and metalaxyl-M were sown on 2005-09-06. Measured concentration was 282 g TMX/L and 457 g TMX/100 kg seed. The wOSR control seeds received only fludioxonil and metalaxyl-M. Prior history of pesticide use in the fields was reported in another study (T003253-05-REG). Before planting the wOSR, the barley was harvested. Meteorological conditions were recorded during the bee exposures (Tables 5 and 6). Before flowering of the wOSR, four tunnels were set up in the TMX-treated field and two tunnels in the control field. The size of the tunnels was 200 m^2 (Figure 2 & 3). For the test, healthy colonies with young bees (1 queen and approx. 10,000 to 20,000 bees per colony) in hives with two boxes (lower box = brood chamber = 1; upper box = honeycomb box = 2) including 10 combs each were used. For the royal jelly production, colonies with approximately 20,000 to 30,000 bees and two boxes including 10 combs each were used. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases (certified in good health). The hives were introduced into the tunnels at the start of flowering (2006-05-01; BBCH 60-62). The hives were left in the tunnels for 13 d after set up. Thereafter, bees were maintained in the forest of Haguenau, Alsace, approximately 450 km away from the field site. Forager bees were collected on 2, 8 and 10 d after initial exposure. The entrance of the hive was sealed and forager bees collected as they returned to the hive by brushing them into a box filled with dry ice. The bees were stored deep-frozen (≤-18C) in one container for each treatment, each sampling time and each sub-sample until the preparation of the honey stomachs and pollen loads. Collection of pollen and nectar from bees was conducted at the LAVES Bee Institute in Celle, Germany. After thawing for a few minutes, pollen loads of single bees from the same sub-sample were removed and pooled. The bees and pollen were transferred back to the freezer immediately after	**4**

Responses 1-7: Quality of methods		Score
	the preparation of one sub-sample. To collect nectar, all bees of one sub-sample were thawed for a few minutes. Individual bees were held at thorax and their abdomens were stretched flat with forceps. The abdomen or tergite plates of each bee were removed, so that the honey stomach was freed and held at the lowest part of the esophagus. The honey stomach was then removed and the nectar collected into a vial. All nectar from single bees from the same sub-sample was pooled and samples were stored deep-frozen at ≤-18C. Pollen, nectar, honey, and new and old wax samples were collected from the comb on days -1, 2, 8, 10 and 20 after initial exposure and then monthly until day 139 (2006-09-18). For pollen, nectar, and wax, 3 samples of comb were collected from each hive on each sampling day (except DAE -1), and where possible, pieces of comb containing all three constituents were cut using a clean knife. Honey samples were only taken from capped cells by cutting a section of comb. Samples were chilled during transport to the freezer but were then stored at ≤-18C. Royal jelly was collected on days 3, 6 and 8 d after initial exposure. This was done in the hive in the additional tunnel. The combs were manipulated to ensure that the royal jelly was fresh. On each sampling day, after the cups with royal jelly were removed, new queen cups containing young larvae, were inserted in the colonies. Two and a half days later the produced royal jelly was sampled. All samples were stored deep-frozen at ≤-18C. Samples were shipped to Syngenta in the UK for analysis using standard methods. Temperatures were recorded during shipping (Table 36). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure. The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery(%RSD) was 90(17%) and 87(13%) respectively (data from Table 5, p. 18, T020431-04-REG). For nectar from bees, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 94(12%) and 95(7%) respectively (data from Table 6, p 18, T020431-04-REG). For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 86(19%) and 86(22%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 87(15%) and 78(13%) respectively. For nectar from the comb LOQs were 0.5 and 1 µg/kg respectively; recovery was 103(6%) and 93(11%) respectively (data from Tables 6-8, p 20, CEMS-3063). For honey from the comb, LOQs were 0.5 and 1 µg/kg respectively; recovery was 101(0%) and 101(3%) respectively, and for royal jelly, LOQs were 0.5 and 1 µg/kg respectively; recovery was 120(24%) and 93(3%) respectively (data from Table 9, p 21, CEMS-3063). Residues were not detected in any of the control samples, in the wax, in the honey and nectar from the comb or in the royal jelly. Samples of whole plants were also collected and clothianidin was detected in one of the samples of wOSR plants (Table 1 in T020431-04-REG).	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**

Responses 1-7: Quality of methods			Score
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control. There was one replicate treatment (tunnel) and one control tunnel for the collection of royal jelly.		**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.		**4**
Overall evaluation of methods	Computed mean of above		**3.4**
Score for expert judgment on Quality of the study.		**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from wOSR grown from seeds treated with TMX in Picardie (data T020431-04-REG; p 16-17 and p 12-19 in CHEMS-3063)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in pollen collected by bees (n = 27)	0.0	0.0	8.6	Larva	124
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in nectar collected by bees (n = 27)	2.2	0.6	8.6	Adult	292
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in wax from hive (n = 45)	0.0	NA	8.6	NA	NA
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in pollen from hive (n = 45)	3.3	0.4	8.6	Larva	124
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in nectar from hive (n = 45)	0.0	0.0	8.6	Adult	292
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in honey from hive (n = 16)	0.0	0.0	8.6	Adult	292
wOSR grown from treated seed in soil where barley with treated seed had been grown.	max. in royal jelly from hive (n = 9)	0.0	0.0	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees resulted in exposures that were less than the NOAED for honeybees.	**0**

Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from the hive resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 7: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in royal jelly produced by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016

SEJ	Yes	May 29, 2016

(Syngenta 2007c)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A Residue Study with A9807C Treated Winter Oil-Seed Rape Seed, Investigating Residues in Crop and Honeybee Products in Alsace (France). Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA173506_7186 A9807C. 152 p

The objective of the study was to determine the concentration of TMX and its metabolite clothianidin in crop and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for winter oilseed rape (wOSR).

Responses 1-7: Quality of methods		**Score**
Experimental design and hypotheses	The methods used in this study were well described. The site was at Meistratzheim in Alsace, France and the study was conducted in 2004-2005. The treated field was 1.6 ha and the control was 1.9 ha. Distance between the fields was not reported but is not relevant as this was a tunnel study. The wOSR seeds (var. Roxet) were treated with CGA173506/ CGA293343/ CGA329351 FS containing TMX, fludioxonil, and metalaxyl-M. Measured concentration was 282 g TMX/L and the concentration measured in the seeds was 440 g/100 kg seed (p 72). The control seeds received only thiram. Seeds were planted 2004-09-13. Prior history of pesticide use in the fields was reported in another study (20041365/F1-BFEU). Meteorological conditions were recorded during the exposures of the bees (Table 5 and Table 6 in Appendix A1). Before flowering of the wOSR, four tunnels were set up in the TMX-treated field and two tunnels in the control field. The size of the tunnels was 200 m^2 (Figure 2). For the test, healthy colonies with young bees (1 queen and approx. 10,000 to 20,000 bees per colony) in hives with two boxes (lower box = brood chamber = 1; upper box = honeycomb box = 2) including 10 combs each were used. For the royal jelly production, colonies with approximately 20,000 to 30,000 bees and two boxes including 10 combs each were used. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases (certified in good health). The hives were introduced into the tunnels at the start of flowering (2005-04-28; BBCH 60–62). The hives were left in the tunnels for 14 d after set up. Thereafter, bees were maintained Wissembourg, Alsace, approx. 75 km away from the field site. Forager bees were collected on 3, 10, and 12 d after initial exposure. The entrance of the hive was sealed and ca. 300 forager bees collected as they returned to the hive by brushing them into a box filled with dry ice. The bees were stored deep-frozen (≤-18C) in one container for each treatment, each sampling time and each sub-sample until the preparation of the honey stomachs and pollen loads, which was done in Celle, Germany. After thawing for a few minutes, pollen loads of single bees from the same sub-sample were removed and pooled. The bees and pollen were transferred back to the freezer immediately after the preparation of one sub-sample. To collect nectar, all bees of one sub-sample were thawed for a few minutes. Individual bees were held at thorax and their abdomens were stretched flat with forceps. The abdomen or tergite plates of each bee were removed, so that the honey stomach was freed and held at the lowest part of the	**4**

Responses 1-7: Quality of methods		Score
	esophagus. The honey stomach was then removed and the nectar collected into a vial. All nectar from forager bees from each subsample was pooled and samples were stored deep-frozen at ≤-18C. Pollen, nectar, honey, and wax samples were collected from the comb on days -1, 3, 10, 12, and 21 after initial exposure and monthly thereafter until mid-September 2005. For pollen, nectar, and wax, 3 samples of comb were collected from each hive on each sampling day, by cutting pieces of comb containing pollen and nectar using a clean knife. Honey samples, collected at the same time as pollen, nectar and wax were distinguished from nectar based on having a water content of less than 20% (measured with a refractometer). Samples were chilled during transport to the freezer but were then stored at ≤-18C. Royal jelly was collected on days 5, 8 and 10 d after initial exposure. This was done in the hive in the additional tunnel. The combs were manipulated to ensure that the royal jelly was fresh. On each sampling day, after the cups with royal jelly were removed, new queen cups containing young larvae, were inserted in the colonies. Two to three days later the produced royal jelly was sampled. All samples were stored deep-frozen at ≤-18C. Samples of whole plants were also collected and residues of TMX and clothianidin were detected (Appendix A3, Table 2). Samples were shipped to Syngenta in the UK for analysis using standard methods. Temperatures were recorded during shipping (Table 43, p 70). The extractions and sample preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure. The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery(%RSD) was 102(4%) and 92(14%). For nectar from bees, the LOQs were 0.5 and 1 µg/kg resp.; recovery was 100(13%) and 96(11%) respectively. For wax, the LOQs were 0.5 and 1 µg/kg resp.; recovery was 99(18%) and 103(23%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 91(18%) and 94(17%) resp. For nectar from the comb LOQs were 0.5 and 1 µg/kg resp.; recovery was 94(9%) and 95(8%) respectively. For honey from the comb, LOQs were 0.5 and 1 µg/kg resp.; recovery was 91(9%) and 97(11%) resp., and for royal jelly, LOQs were 0.5 and 1 µg/kg respectively; recovery was 97(11%) and 82(18%) respectively (data Tables 11 to 17). Residues were not detected in any of the control samples, in the wax, in the honey and nectar from the comb or in the royal jelly. Clothianidin was not detected in any bee-relevant matrices.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some of the meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**

Responses 1-7: Quality of methods		Score
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of TMX in bee-relevant matrices from wOSR grown from seeds treated with TMX in Alsace (data from Report RJ3775B Tables 3 to 9)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR grown from treated seed.	max. in pollen collected by bees (n = 27)	4.0	0.5	8.6	Larva	124
wOSR grown from treated seed.	max. in nectar collected by bees (n = 27)	4.0	1.2	8.6	Adult	292
wOSR grown from treated seed.	max. in wax from hive (n = 62)	0.0	NA	8.6	NA	NA
wOSR grown from treated seed.	max. in pollen from hive (n = 50)	3.0	0.37	8.6	Larva	124
wOSR grown from treated seed.	max. in nectar from hive (n = 55)	0.0	0.0	8.6	Adult	292
wOSR grown from treated seed.	max. in honey from hive (n = 33)	0.0	0.0	8.6	Adult	292
wOSR grown from treated seed.	max. in royal jelly from hive (n = 9)	0.0	0.0	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax in the hive resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 7: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in royal jelly produced by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007d)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A Residue Study with A9807C Treated Winter Oil-Seed Rape Seed, Investigating Residues in Crop and Honeybee Products in Southern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA173506_7188 A9807C. 126 p

The objective of the study was to determine the concentration of TMX and its metabolite clothianidin in crop and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for winter oilseed rape (wOSR).

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods used in this study were well described. The site was near Toulouse in the region of Midi-Pyrénées, France and the study was conducted in 2004-2005. The treated field was 1.5 ha and the control was 1.4 ha. Distance between the fields was not reported but is not relevant as this was a tunnel study. The wOSR seeds (var. Roxet) were treated with CGA173506/ CGA293343/ CGA329351 FS containing TMX, fludioxonil, and metalaxyl-M. Measured concentration was 282 g TMX/L and the concentration measured in the seeds was 450 g/100 kg seed (p 68). The control seeds received only thiram. Seeds were planted 2004-09-10. Prior history of pesticide use in the fields was reported in another study (20041365/F1BFEU). Meteorological conditions were recorded with a data logger and from a local weather station (non-GLP) during the exposures of the bees (Table 5 and 6 in Appendix A1). Before flowering of the wOSR, three tunnels were set up in the TMX-treated field and one tunnel in the control field. The size of the tunnels was 200 m^2 (Figure 2). For the test, healthy colonies with young bees (1 queen and approx. 10,000 to 20,000 bees per colony) in hives with two boxes (lower box = brood chamber = 1; upper box = honeycomb box = 2) including 10 combs each were used. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases (certified in good health). The hives were introduced into the tunnels at the start of flowering (BBCH 60–62). The hives were placed in the tunnels on 2005-04-07 and left in the tunnels for 10 d after set up. Thereafter, bees were maintained Gers, Le Marteret, Midi-Pyrénées approx. 70 km away from the field site. Forager bees were collected on 4, 6, and 9 d after initial exposure. The entrance of the hive was sealed and ca. 300 forager bees collected as they returned to the hive by brushing them into a box filled with dry ice. The bees were stored deep-frozen (≤-18C) in one container for each treatment, each sampling time and each sub-sample until the preparation of the honey stomachs and pollen loads, which was done in Celle, Germany. After thawing for a few minutes, pollen loads of single bees from the same sub-sample were removed and pooled. The bees and pollen were transferred back to the freezer immediately after the preparation of one sub-sample. To collect nectar, all bees of one sub-sample were thawed for a few minutes. Individual bees were held at thorax and their abdomens were stretched flat with forceps. The abdomen or tergite plates of each bee were removed, so that the honey stomach was freed and held at the lowest part of the	**4**

Responses 1-6: Quality of methods		Score
	esophagus. The honey stomach was then removed and the nectar collected into a vial. All nectar from forager bees from the same sub-sample was pooled and samples were stored deep-frozen at ≤-18C. Pollen, nectar, honey, and old and new wax samples were collected from the comb on days -1, 4, 6, 9, and 19 after initial exposure and monthly thereafter until mid-September 2005. For pollen, nectar, and wax, 3 samples of comb were collected from each hive on each sampling day, by cutting pieces of comb containing pollen and nectar using a clean knife. Honey samples, collected at the same time as pollen, nectar and wax were distinguished from nectar based on having a water content of less than 20% (measured with a refractometer). Samples were chilled during transport to the freezer but were then stored at ≤-18C. All samples were stored deep-frozen at ≤-18C. Samples of whole plants were also collected and residues of TMX and clothianidin were detected (Appendix A3, Table 2, analytical report). Samples were shipped to Syngenta in the UK for analysis using standard methods. Temperatures were recorded during shipping (Table 41, Appendix A1). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure. The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery(%RSD) was 80(12%) and 87(16%). For nectar from bees, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 85(12%) and 88(7%) respectively. For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 91(16%) and 83(26%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 89(11%) and 91(11%) respectively. For nectar from the comb LOQs were 0.5 and 1 µg/kg respectively; recovery was 92(12%) and 91(13%) respectively. For honey from the comb, LOQs were 0.5 and 1 µg/kg respectively; recovery was 92(9%) and 90(11%) respectively (data Tables 10 to 15 of the Analytical Report). Residues were not detected in any of the control samples, in the wax, and in the honey from the comb. Clothianidin was not detected in any bee-relevant matrices.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some of the meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of TMX in bee-relevant matrices from wOSR grown from seeds treated with TMX near Toulouse (data from Report RJ3772B, Tables 3 to 8)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR grown from treated seed.	max. in pollen collected by bees (n = 27)	4.0	0.5	8.6	Larva	124
wOSR grown from treated seed.	max. in nectar collected by bees (n = 27)	4.0	1.2	8.6	Adult	292
wOSR grown from treated seed.	max. in wax from hive (n = 50)	0.0	NA	8.6	NA	NA
wOSR grown from treated seed.	max. in pollen from hive (n = 54)	2.0	0.25	8.6	Larva	124
wOSR grown from treated seed.	max. in nectar from hive (n = 52)	0.9	0.3	8.6	Adult	292
wOSR grown from treated seed.	max. in honey from hive (n = 33)	0.0	0.0	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax in the hive resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007a)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A residue study with A10590C treated maize seed, investigating residues in crop, soil and honeybee products in Alsace, France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA173506_7323 - A10590C (20051149/F1-BZEU). 149 p

The objective of the study was to determine concentrations of TMX and its metabolite clothianidin in crop, soil and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for maize. The study was conducted in two years and relevance for each year was scored separately.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods for this study were well described. The study took place over two years (2005-2006) with treated seed planted each year. The test took place in Zellwiller, Alsace, France. The cropping and pesticide use in the field was provided (Tables 5 and 6) and no neonicitinoids were used in the prior three years. The test and control plots were 0.4 ha each and sowing was on 2005-05-13 and 2006-05-04. A Monosem pneumatic drill was used in both years at a rate of 28 kg seed/ha. Seeds of *Zea mays* (var. Delitop (2005) and Moncada (2006)) were treated with CGA173506/CGA293343/ CGA329351 FS, containing TMX (analyzed 417 and 403 g/L in 2005 and 2006, respectively; application rate of 89.3 g a.s./ha and 85.8 g a.s./ha in 2005 and 2006, respectively), fludioxonil, and metalaxyl-M. Measured concentrations in treated seed were 321 g/100 kg for 2005 and 326 g/100 kg for 2006 (Sections 4.2.2 and 4.2.3 and p 76 & 78). Control seed (same var.) was untreated in both years. Weather conditions were recorded from local instruments and nearby weather stations (non-GLP) (see Tables 13-15). Prior to flowering, three tunnels (200 m^2) were set up on the test plot and one on the control (Figures 2 and 3). Bees were used to collect pollen. Healthy colonies with young bees (1 queen and approx. 10,000 to 20,000 bees per colony) in hives with two boxes (lower box = brood chamber = 1; upper box = honeycomb box = 2) including 10 combs each were used. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases. The hives were introduced into the tunnels at BBCH stage 63 on 2005-07-18 and 2006-07-17. In 2005 bees were left in the tunnels for 10 d and in 2006 for 4 d. In both years, bees were moved to Haguenau, approx. 55 km away from the field site after exposures ceased. Soil was sampled in May 2006 (post-harvest of 2005 crop but pre-drilling of the 2006 crop) for soil characterization and residue analysis and maize plants were sampled for residue analysis in both years. TMX and clothianidin were detected in maize plants in both years but not in soil in 2006 (LOQ = 1 µg/kg). Pollen was collected from forager bees on three days in 2005 and 2006. The entrance to the hive was sealed and returning foragers were collected with forceps and frozen on dry ice. Bees were then stored at -18C. The preparation of the bee samples was conducted by at LAVES Bee Institute in Celle, Germany. After thawing, pollen loads of single bees from the same subsample were removed, pooled, and then stored at -18C. Samples of pollen	**4**

Responses 1-6: Quality of methods		Score
	and wax from the combs were collected in both years. For pollen and wax, 3 samples of comb were collected from each hive on each sampling day (except DAE -1 in 2006), by cutting pieces of comb containing pollen using a clean knife. In 2005 samples of comb were taken on -1, 4, 5, 7, 20, 31, and 50 d after initial exposure. In 2006, they were taken on -1, 2, 3, 21, and 48 d after initial exposure. In addition to bee-collected pollen in 2006, pollen from maize was collected by hand 1, 2 and 3 d after initial exposure. The tassel of a maize plant was placed in a plastic bag and shaken for a few seconds in order to break the anthers, resulting in pollen-shed. This was done for at least five plants at each of 12 different locations in each of the tunnels. All samples were frozen at -18C and shipped frozen to Syngenta UK for analysis. Storage and shipments conditions were recorded using a data logger and a minimax. thermometer (see Tables 50 and Table 51 in the Appendix A1 for details). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure (Appendix A4/A5). The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery(%RSD) was 91(16%) and 92(24%) data from Table 9 in T020433-04-REG (Appendix A4). For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 93(11%) and 95(14%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 90(13%) and 96(18%) respectively (data Tables 4 and 5 in CEMR-2943, Appendix A5). Residues were not detected in any of the control samples, in the wax, and pollen from the comb. Clothianidin was not detected in wax but was in pollen from the hive and collected by bees.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some of the meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from maize grown from seeds treated with TMX near Alsace (data from Tables 4 to 6 in Appendix A4 and Tables 1 to 3 in Appendix A5)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize grown from treated seed 2005.	max. in pollen collected by bees (n = 23)	19.0	2.4	8.6	Larva	124

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from maize grown from seeds treated with TMX near Alsace (data from Tables 4 to 6 in Appendix A4 and Tables 1 to 3 in Appendix A5)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize grown from treated seed 2005.	max. in pollen from hive (n = 50)	11.0	1.4	8.6	Larva	124
Maize grown from treated seed 2005.	max. in wax from hive (n = 63)	0.0	NA	8.6	NA	NA
Maize grown from treated seed 2006.	max. in pollen collected by bees (n = 12)	4.3	0.5	8.6	Larva	124
Maize grown from treated seed 2006.	max. in wax from hive (n = 44)	0.0	NA	8.6	NA	NA
Maize grown from treated seed 2006.	max. in pollen from plants (n = 43)	0.0	0.00	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees in 2006 resulted in exposures that were less than the NOAED for honeybees.	**0**

Response 4: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive in 2006 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from maize plants in 2006 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007f)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A residue study with A10590C treated maize seed, investigating residues in crop, soil and honeybee products in Southern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA173506_7324 - A10590C (20051149/F2-BZEU). 154 p

The objective of the study was to determine concentrations of TMX and its metabolite clothianidin in crop, soil and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for maize. The study was conducted in two years and relevance for each year was scored separately.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods for this study were well described. The study took place over two years (2005-2006) with treated seed planted each year in Grisolles, near Toulouse, Midi-Pyrenees, France. The previous cropping and pesticide use in the field was provided (Tables 6 and 7) and no neonicotinoids were used in the prior two years. The test and control plots were 0.4 ha each and sowing was on 2005-05-04 and 2006-05-10. A Khun pneumatic drill was used in both years at a rate of 28 kg seed/ha. Seeds of *Zea mays* (var. NK Terra (both years) were treated with CGA173506/CGA293343/ CGA329351 FS, containing TMX (analyzed 417 and 403 g/L in 2005 and 2006, respectively; application rate of 90.4 g a.s./ha and 84.6 g a.s./ha in 2005 and 2006, respectively), fludioxonil, and metalaxyl-M. Measured concentrations in treated seed were 328 g/100 kg for 2005 and 317 g/100 kg for 2006 (Sections 4.2.2 and 4.2.3 and p 80 & 82). Control seed (same var.) was untreated in both years. Weather conditions were recorded from local instruments and nearby weather stations (non-GLP) (see Tables 12-16). Prior to flowering, three tunnels (200 m^2) were set up on the test plot and one on the control (Figures 2-4). Bees were used to collect pollen. Healthy colonies with young bees (1 queen and approx. 10,000 to 20,000 bees per colony) in hives with two boxes (lower box = brood chamber = 1; upper box = honeycomb box = 2) including 10 combs each were used. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases. The hives were introduced into the tunnels at BBCH stage 63. In both years, bees were placed in the tunnel on 2005-07-13 and left for 9 d. Bees were moved to le Marteret, Biran (in 2005) and in Louslitges (in 2006); 90 and 100 km away from the field site, after exposures ceased. Soil was sampled in May 2006 (post-harvest of 2005 crop but pre-drilling of the 2006 crop) for soil characterization and residue analysis and maize plants were sampled for residue analysis in both years. TMX and clothianidin were detected in maize plants in both years and only clothianidin was detected in soil in 2006 (LOQ = 1 µg/kg). Pollen was collected from forager bees on three days in 2005 and 2006. The entrance to the hive was sealed and returning foragers were collected with forceps and frozen on dry ice. Bees were then stored at -18C. The preparation of the bee samples was conducted by at LAVES Bee Institute in Celle, Germany. After thawing, pollen loads of single bees from the same subsample were removed, pooled and then stored at -	**4**

Responses 1-6: Quality of methods		Score
	18C. Samples of pollen and wax from the combs were collected in both years. For pollen and wax, 3 samples of comb were collected from each hive on each sampling day (except DAE -1 in 2006), by cutting pieces of comb containing pollen using a clean knife. In 2005 samples of comb were taken on 0, 3, 4, 5, 8, 20, 31, and 54 d after initial exposure. In 2006, they were taken on -1, 2, 3, 4, 5 21, 50, and 77 d after initial exposure. In addition to bee-collected pollen in 2006, pollen from maize was collected by hand 3, 4, and 5 d after initial exposure. The tassel of a maize plant, collected in the morning, was placed in a plastic bag and shaken for a few seconds to break the anthers, resulting in pollen-shed. This was done for at least five plants at each of 12 different locations in each of the tunnels. All samples were frozen at -18C and shipped frozen to Syngenta UK for analysis. Storage and shipments conditions were recorded using a data logger and a minimax. thermometer (see Tables 48 and Table 49 in the Appendix A1 for details). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure (Appendix A4/A5). The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery(%RSD) was 84(20%) and 93(21%) data from Table 8 in T003255-05-REG (Appendix A4). For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 94(9%) and 96(11%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 94(11%) and 94(13%) respectively (data Tables 5 and 6 in CEMR-2943, Appendix A5). Residues were not detected in any of the control samples. Clothianidin was not detected in wax but was in pollen from the hive and collected by bees.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some of the meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from maize grown from seeds treated with TMX near Toulouse (data from Tables 4 and 5 in Appendix A4 and Tables 1 to 4 in Appendix A5)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize grown from treated seed 2005.	max. in pollen collected by bees (n = 27)	13.2	1.63	8.6	Larva	124

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from maize grown from seeds treated with TMX near Toulouse (data from Tables 4 and 5 in Appendix A4 and Tables 1 to 4 in Appendix A5)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize grown from treated seed 2005.	max. in pollen from hive (n = 49)	3.2	0.4	8.6	Larva	124
Maize grown from treated seed 2005.	max. in wax from hive (n = 57)	0.9	NA	8.6	NA	NA
Maize grown from treated seed 2006.	max. in pollen collected by bees (n = 14)	11.4	1.4	8.6	Larva	124
Maize grown from treated seed 2006.	max. in wax from hive (n = 44)	0.0	NA	8.6	NA	NA
Maize grown from treated seed 2006.	max. in pollen from plants (n = 49)	1.0	0.12	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees in 2006 resulted in exposures that were less than the NOAED for honeybees.	**0**

Response 4: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive in 2006 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from maize plants in 2006 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007g)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A residue study with A10590C treated maize seed, investigating residues in crop, soil and honeybee products in northern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA173506_7333 - A10590C (2032750). 127 p

The objective of the study was to determine concentrations of TMX and its metabolite clothianidin in crop, soil and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for maize. The study was conducted in two years and relevance for each year was scored separately.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods for this study were well described. The study took place over two years (2005-2006) with treated seed planted each year in Champagne, France. The cropping and pesticide use in the field was provided (Appendix 3) and no neonicotinoids were used in the prior two years. The test and control plots were approx. 0.5 ha each and sowing was on 2005-05-10 and 2006-05-04. Nodet Gougis 6 row pneumatic precision drill was used in both years at a rate of 27 kg seed/ha. Seeds of *Zea mays* (var. Delitop (2005) and Moncada (2006) were treated with CGA173506/CGA293343/ CGA329351 FS, containing TMX (analysed 417 and 403 g/L in 2005 and 2006, respectively), fludioxonil, and metalaxyl-M. Measured concentrations in treated seed were 321 g/100 kg for 2005 and 319 g/100 kg for 2006 (p 15). Control seed (same var.) was untreated in both years. Weather conditions were recorded from a nearby weather station (non-GLP, see Table 11) and locally recorded weather data; Appendix 3). Prior to flowering, three tunnels (180 m^2) were set up on the test plot and one on the control. Bees (*Apis mellifera* L.) were used to collect pollen. Healthy colonies were medium sized, queen right (approx. 10,000 to 20,000 bees per colony). The colonies had at least 4-5 brood combs containing all brood stages and at least 2-3 honey and pollen combs. Each colony was contained in two brood boxes, which in total contained 18 combs. The condition of the colonies was assessed prior to the introduction into the tunnels and again at the end of flowering/honeybee exposure (before removal to the remote location). The hives were introduced into the tunnels at BBCH stage 61/63. In 2005, bees were placed in the tunnels on 2005-07-20 and left for 6 d. In 2006, bees were placed in the tunnel on 2006-07-18 and left for 5 d. Bees from the control colonies went to the forest in Stiefelhardt and treated colonies went to the forest in Mertzwiller in each year after exposures ceased. Soil was sampled in April 2006 (post-harvest of 2005 crop but pre-drilling of the 2006 crop) for soil characterization and residue analysis and maize plants were sampled for residue analysis in both years. TMX and clothianidin were detected in maize plants in both years but only clothianidin was detected in soil in 2006 (LOQ = 1 µg/kg Appendix 4 Tables 1-3). Pollen was collected from forager bees on three days in 2005 and 2006. The entrance to the hive was sealed and returning foragers were collected and frozen on dry ice. Bees were then stored at -18C. The preparation of the bee samples was conducted at	**4**

Responses 1-6: Quality of methods		Score
	Syngeta's Jealott's Hill UK Research Centre. After thawing, pollen was removed and then stored at -18C. Samples of pollen and wax from the combs were collected in both years. For pollen and wax, 3 samples of comb were collected from each hive on each sampling day (except DAE -1 in 2006), by cutting pieces of comb containing pollen using a disposable plastic knife. In 2005 samples of comb were taken on -1, 2, 3, 4, 21, 49 d after initial exposure. In 2006, they were taken on -1, 2, 3, 4, 21, 48 d after initial exposure. All samples were frozen at -18C and shipped frozen to Syngenta UK for analysis. Storage and shipments conditions were recorded using a data logger and a minimax. thermometer (see Tables 12 and Table 13). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure (Appendix 4). The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery(%RSD) was 88(18%) and 88(11%). For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 99(10%) and 90(17%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 87(12%) and 84(19%) respectively (data from Appendix 4, Tables 12–14). Residues were not detected in any of the control samples. Clothianidin was not detected in wax but was in pollen from the hive and pollen collected by bees.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some of the meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from maize grown from seeds treated with TMX near Champagne (data from Tables 4 to 9 in Appendix 4)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize grown from treated seed 2005.	max. in pollen collected by bees (n = 27)	7.5	0.9	8.6	Larva	124
Maize grown from treated seed 2005.	max. in pollen from hive (n = 27)	5.5	0.7	8.6	Larva	124
Maize grown from treated seed 2005.	max. in wax from hive (n = 54)	1.4	NA	8.6	NA	NA

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from maize grown from seeds treated with TMX near Champagne (data from Tables 4 to 9 in Appendix 4)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize grown from treated seed 2006.	max. in pollen collected by bees (n = 27)	4.3	0.5	8.6	Larva	124
Maize grown from treated seed 2006.	max. in pollen from hive (n = 36)	2.2	0.3	8.6	Larva	124
Maize grown from treated seed 2006.	max. in wax from hive (n = 39)	0.0	NA	8.6	NA	NA

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive in 2005 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees in 2006 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive in 2006 resulted in exposures that were less than the NOAED for honeybees.	**0**

Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive in 2006 resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007h)
Report: Syngenta. 2007. Thiamethoxam (CGA293343) and its Metabolite (CGA322704): A Residue Study with A9700B Treated Spring Barley Seed Followed by A9807C Treated Winter Oil-Seed Rape Seed, Investigating Residues in Crop, Soil and Honeybee Products in Southern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_ 3436 A9700B, A9807C (20051040/F2-BZEU). 160 p

The objective of the study was to determine the concentration of TMX and its metabolite clothianidin in crop and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for spring barley followed by winter oilseed rape (wOSR).

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods used in this study were well described. The site was Ondes, near Toulouse in Midi-Pyrenees, France and the study was conducted in 2005-2006. The treated field was 0.5 ha and was sown on 2005-03-07 with seeds of spring barley (var. Astoria) treated with CGA293343 FS (350) A9700B analyzed at 354 g TMX/L and 720 g TMX/100 kg seed. Spring barley control seeds were untreated. The wOSR seeds (var. Roxet) were treated with CGA173506/ CGA293343/ CGA329351 FS (A9807C) containing TMX, fludioxonil, and metalaxyl-M. Measured concentration was 282 g TMX/L and 457 g TMX/100 kg seed. The wOSR control seeds received only fludioxonil and metalaxyl-M. Seeding of barley with a Nodet Gougis mechanical drill on 2005-03-07 and wOSR with a Khun pneumatic drill on 2005-09-19. Prior history of pesticide use in the fields was reported in Tables 6 and 7 (Section 4.2.6). Before planting the wOSR, the barley was harvested. Meteorological conditions were recorded during the bee exposures (Tables 11 and 13 in Appendix A1). Before flowering of the wOSR, three tunnels were set up in the TMX-treated field and one tunnel in the control field. The size of the tunnels was 200 m^2 (Figures 2 & 3). For the test, healthy colonies with young bees (1 queen and approx. 6,000 to 7,000 bees per colony) in hives with one box including 10 combs. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases. The hives were introduced into the tunnels at the start of flowering (2006-04-06; BBCH 60–62). The hives were left in the tunnels for 11 d after set up. Thereafter, bees were maintained in Louslitges, Midi-Pyrenees, approximately 100 km away from the field site. Forager bees were collected on 1, 7 and 9 d after initial exposure. The entrance of the hive was sealed and forager bees collected as they returned to the hive by brushing them into a box filled with dry ice. The bees were stored deep-frozen (≤-18C) in one container for each treatment, each sampling time and each sub-sample until the preparation of the honey stomachs and pollen loads. Collection of pollen and nectar from bees was conducted at the LAVES Bee Institute in Celle, Germany. After thawing for a few minutes, pollen loads of single bees from the same sub-sample were removed and pooled. The bees and pollen were transferred back to the freezer immediately after the preparation of one sub-sample. To collect nectar, all bees of one sub-sample were thawed for a few minutes. Individual bees were held at thorax and their abdomens were stretched flat with forceps. The	**4**

Responses 1-6: Quality of methods		Score
	abdomen or tergite plates of each bee were removed, so that the honey stomach was freed and held at the lowest part of the esophagus. The honey stomach was then removed and the nectar collected into a vial. All nectar from single bees from the same sub-sample was pooled and samples were stored deep-frozen at ≤-18C. Pollen, nectar, honey, and wax samples were collected from the comb on days -1, 1, 7, 9 and 20 after initial exposure and then monthly until day 174 (2006-09-28). For pollen, nectar, and wax, 3 samples of comb were collected from each hive on each sampling day (except DAE -1), and where possible, pieces of comb containing all three constituents were cut using a clean knife. Honey samples were only taken from capped cells by cutting a section of comb. Samples were chilled during transport to the freezer but were then stored at ≤-18C. All samples were stored deep-frozen at ≤-18C. Soil was sampled in 2005-09-16 (post-harvest of spring barley but pre-drilling of wOSR) for soil characterization and residue analysis and whole wOSR plants were sampled for residue analysis. Samples were shipped to Syngenta in the UK for analysis using standard methods. Temperatures were recorded during shipping (p 35–36). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure. The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg respectively and recovery(%RSD) was 78(22%) and 89(11%) respectively (Table 7 in T003254-05-REG). For nectar from bees, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 88(14%) and 98(18%) respectively (Table 8 in T003254-05-REG). For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 97(13%) and 89(25%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 100(17%) and 100(10%) respectively. For nectar from the comb LOQs were 0.5 and 1 µg/kg respectively; recovery was 101(22%) and 88(14%) respectively (data from Tables 5-7, p 19, CEMS-3062). For honey from the comb, LOQs were 0.5 and 1 µg/kg respectively; recovery was 92(19%) and 88(11%) respectively, (data from Table 8, p 20 in CEMS-3062). Residues of TMX and clothianidin were detected in wOSR plants and in soil in 2006 (LOQ = 1 µg/kg, Appendix A4 (T003254-05-REG), Tables 1 & 2). Residues of TMX or clothianidin were not detected in any of the control samples.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from wOSR grown from seeds treated with TMX in Ondes, near Toulouse (data from T003254-05-REG; p 17-18 and p 12-18 CHEMS-3062)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in pollen collected by bees (n = 24)	8.3	1.0	8.6	Larva	124
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in nectar collected by bees (n = 27)	4.6	1.3	8.6	Adult	292
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in wax from hive (n = 44)	0.9	NA	8.6	NA	NA
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in pollen from hive (n = 54)	4.2	0.52	8.6	Larva	124
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in nectar from hive (n = 51)	2.5	0.7	8.6	Adult	292
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in honey from hive (n = 30)	0.8	0.2	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax from the hive resulted in exposures that were assumed to be less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from the hive resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007i)
Report: Syngenta. 2007. Thiamethoxam (CGA 293343) and its Metabolite (CGA322704): A Residue Study with A9700B Treated Spring Barley Seed Followed by A9807C Treated Winter Oilseed Rape Seed, Investigating Residues in Crop, Soil and Honeybee Products in Northern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343-3456 A9700B, A9807C (2032738). 182 p

The objective of the study was to determine the concentration of TMX and its metabolite clothianidin in crop and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for spring barley followed by winter oilseed rape (wOSR).

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods used in this study were well described. The site was Beine Nauroy, Champagne, France and the study was conducted in 2005-2006. The treated field was 0.5 ha and was sown on 2005-03-18 with seeds of spring barley (var. Astoria) treated with CGA293343 FS (350) A9700B analyzed at 354 g TMX/L and 700 g TMX/100 kg seed. Spring barley control seeds were untreated. The wOSR seeds (var. Roxet) were treated with CGA173506/ CGA293343/ CGA329351 FS (A9807C) containing TMX, fludioxonil, and metalaxyl-M. Measured concentration was 282 g TMX/L and 420 g TMX/100 kg seed. The wOSR control seeds received only fludioxonil and metalaxyl-M. Seeding of barley with a mechanical drill on 2005-03-18 and wOSR with a Monosem pneumatic drill on 2005-08-31. Prior history of pesticide use in the fields was reported in Tables 4.2.3 and 4.2.4 in Appendix 2. Before planting the wOSR, the barley was harvested. Meteorological conditions were recorded during the bee exposures (Table 11 and Appendix 2). Before flowering of the wOSR, three tunnels were set up in the TMX-treated field and one tunnel in the control field. The size of the tunnels was 200 m^2. The colonies used in the test were medium sized, queen-right and contained 10,000–20,000 bees (*Apis mellifera* L.). The colonies had at least 4-5 brood combs containing all brood stages and honey and pollen combs. Each colony was contained in two brood boxes, which, in total, contained 20 combs. The hives were introduced into the tunnels at the start of flowering (BBCH 60–62; 2006-05-03). The hives were left in the tunnels for 9 d after set up. Thereafter, bees were maintained in Mertzwiller, Alsace. Forager bees were collected on 2, 7 and 9 d after initial exposure. The entrance of the hive was sealed and forager bees collected as they returned to the hive by brushing them into a box filled with dry ice. The bees were stored deep-frozen (≤-18C) until the preparation of the honey stomachs and pollen loads. Collection of pollen and nectar from bees was conducted Eurofins-GAB GmbH, Celle, Germany. After thawing for a few minutes, pollen loads of single bees from the same sub-sample were removed and pooled. The bees and pollen were transferred back to the freezer immediately after the preparation of one sub-sample. To collect nectar, all bees of one sub-sample were thawed for a few minutes. Individual bees were held at thorax and their abdomens were stretched flat with forceps. The abdomen or tergite plates of each bee were removed, so that the honey stomach was	**4**

Responses 1-6: Quality of methods		Score
	freed. The honey stomach was then removed and the nectar collected into a vial. All nectar from single bees from the same sub-sample was pooled and samples were stored deep-frozen at ≤-18C. Pollen, nectar, honey, and wax (old and new) samples were collected from the comb on days -1, 2, 7, 9, 20, 50, 76, 107, and 138 after initial exposure. For pollen, nectar, and wax, 3 samples of comb were collected from each hive on each sampling day (except DAE -1), and where possible, pieces of comb containing all three constituents were cut using a clean knife. Honey samples (water content <20%) were only taken when available by cutting a section of comb. Samples were chilled during transport to the freezer but were then stored at ≤-18C. All samples were stored deep-frozen at ≤-18C. Soil was sampled in 2005-08-31 (post-harvest of spring barley but pre-drilling of wOSR) for soil characterization and residue analysis and whole wOSR plants were sampled for residue analysis. Samples were shipped to Syngenta in the UK for analysis using standard methods. Temperatures were recorded during shipping (Table 12). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure. The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg respectively and recovery (%RSD) was 94 (8%) and 83 (14%). For nectar from bees, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 103 (6%) and 92 (11%) respectively. For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 95 (11%) and 93 (12%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 81(11%) and 81 (18%) respectively. For nectar from the comb LOQs were 0.5 and 1 µg/kg respectively; recovery was 92 (15%) and 98 (6%) respectively. For honey from the comb, LOQs were 0.5 and 1 µg/kg respectively; recovery was 107 (4%) and 86 (15%) respectively (data from Tables 12-17 in T003253-05-REG). Residues of TMX and clothianidin were detected in wOSR plants and in soil in 2006 (LOQ = 1 µg/kg, Appendix 4 (T003253-05-REG), Tables 1 & 2). Residues of TMX or clothianidin were not detected in any of the control samples, in the wax, the honey, and nectar from the comb.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in bee-relevant matrices from wOSR grown from seeds treated with TMX in Beine Nauroy, Champagne (data from T003253-05-REG; Tables 3-9)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in pollen collected by bees (n = 27)	3.0	0.4	8.6	Larva	124
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in nectar collected by bees (n = 27)	2.4	0.7	8.6	Adult	292
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in old and new wax from hive (n = 60)	0.0	NA	8.6	NA	NA
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in pollen from hive (n = 44)	1.0	0.1	8.6	Larva	124
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in nectar from hive (n = 47)	0.0	0.0	8.6	Adult	292
wOSR grown from treated seed in soil where barley from treated seed had been grown.	max. in honey from hive (n = 14)	0.0	0.0	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees resulted in exposures that were less than the NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**

Response 2: Relevance to adverse effects		Score
Score for expert judgment on relevance of the results.	**1**	**0.00**

Response 3: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in old and new wax from the hive resulted in exposures that were less than the assumed NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**
Score for expert judgment on relevance of the results.	**1**	**0.00**

Response 4: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**
Score for expert judgment on relevance of the results.	**1**	**0.00**

Response 5: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**
Score for expert judgment on relevance of the results.	**1**	**0.00**

Response 6: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey from the hive resulted in exposures that were less than the NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**
Score for expert judgment on relevance of the results.	**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2007j)
Report: Syngenta. 2007. Thiamethoxam (CGA 293343) and its Metabolite (CGA322704): A Residue Study with A9807C Treated Winter Oilseed Rape Seed, Investigating Residues in Crop and Honeybee Products in Northern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA1730506 _7187 A9807C (20051041/F2-BZEU). 152 p

The objective of the semi-field study (tunnels) was to determine the concentration of TMX and its metabolite clothianidin in crop and honeybee products, following use of a flowable concentrate mixture of TMX as a seed treatment for spring winter oilseed rape (wOSR).

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The methods used in this study were well described. The site was near Vingre, Picardie, France and the study was conducted in 2004-2005. The treated field was 2.3 ha and the control was 2 ha. Distance between the fields was not reported but is not relevant as this was a tunnel study. The wOSR seeds (var. Roxet) were treated with CGA173506/ CGA293343/ CGA329351 FS containing TMX, fludioxonil, and metalaxyl-M. Measured concentration was 282 g TMX/L and the concentration measured in the seeds was 440 g/100 kg seed (p 66). The control seeds received only thiram. Seeds were planted 2004-09-08. Prior history of pesticide use in the fields was reported in another study (20041365/F1-BFEU). Meteorological conditions were recorded with a data logger and from a local weather station (non-GLP) during the exposures of the bees (Table 5 and 6 in Appendix A1). Before flowering of the wOSR, three tunnels were set up in the TMX-treated field and one tunnel in the control field. The size of the tunnels was 200 m^2 (Figures 2-4). For the test, healthy colonies with young bees (1 queen and approx. 10,000 to 20,000 bees per colony) in hives with two boxes (lower box = brood chamber = 1; upper box = honeycomb box = 2) including 10 combs each were used. Honeybees (*Apis mellifera* L.) were free of symptoms of *Nosema* and other bee diseases (certified in good health). The hives were introduced into the tunnels at the start of flowering (BBCH 60–62). The hives were placed in the tunnels on 2005-04-26 and left in the tunnels for 10 d after set up. Thereafter, bees were maintained in the forest at Wissembourg, approximately 400 km away from the field site. Forager bees were collected on 2, 5, and 9 d after initial exposure. The entrance of the hive was sealed and ca. 300 forager bees collected as they returned to the hive by brushing them into a box filled with dry ice. The bees were stored deep-frozen (≤-18C) in one container for each treatment, each sampling time and each sub-sample until the preparation of the honey stomachs and pollen loads, which was done in Celle, Germany. After thawing for a few minutes, pollen loads of single bees from the same sub-sample were removed and pooled. The bees and pollen were transferred back to the freezer immediately after the preparation of one sub-sample. To collect nectar, all bees of one sub-sample were thawed for a few minutes. Individual bees were held at thorax and their abdomens were stretched flat with forceps. The abdomen or tergite plates of each bee were removed, so that the honey stomach was freed and held at the lowest part of the	**4**

Responses 1-6: Quality of methods		Score
	esophagus. The honey stomach was then removed and the nectar collected into a vial. All nectar from forager bees from the same sub-sample was pooled and samples were stored deep-frozen at ≤-18C. Pollen, nectar, honey, and old and new wax samples were collected from the comb on days -1, 2, 3, 5, 10, and 22 and then at monthly intervals until 2005-09-20 after initial exposure. For pollen, nectar, and wax, 3 samples of comb were collected from each hive on each sampling day, by cutting pieces of comb containing pollen and nectar using a clean plastic knife. Honey samples, collected at the same time as pollen, nectar and wax were distinguished from nectar based on having a water content of less than 20% (measured with a refractometer). Samples were chilled during transport to the freezer but were then stored at ≤-18C. All samples were stored deep-frozen at ≤-18C. Samples of whole plants were also collected and residues of TMX and clothianidin were not detected (Table 2, report RJ3774B). Samples were shipped to Syngenta in the UK for analysis using standard methods. Temperatures were recorded during shipping (p 24-25 and Table 41, Appendix A1). The extractions and samples preparations were well described. Analysis was by LC MS/MS. Standards were >98% pure. The LOQs for TMX and clothianidin from bee pollen were 1 µg/kg and recovery (%RSD) was 86 (11%) and 89 (6%). For nectar from bees, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 102 (11%) and 98 (10%) respectively (data from Table 6 & 7, report RJ3774B). For wax, the LOQs were 0.5 and 1 µg/kg respectively; recovery was 94 (15%) and 96 (8%) respectively. For pollen from the comb, the LOQs were 1 µg/kg.; recovery was 99 (6%) and 99 (7%) respectively. For nectar from the comb LOQs were 0.5 and 1 µg/kg respectively; recovery was 100 (10%) and 96 (7%) respectively. For honey from the comb, LOQs were 0.5 and 1 µg/kg respectively; recovery was 96 (14%) and 97 (11%) respectively (data Tables 6-9 of the Report CEMS-2898). Residues were not detected in any of the control samples, in the wax, in the honey and nectar from the comb. Clothianidin was not detected in any bee-relevant matrices.	
Use of GLP and QA/QC	This study was conducted under GLP with QA and QC. Some of the meteorological data were not collected under GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site and three replicate treatments (tunnels) and one control.	**1**
Duration of study sufficient to observe trends	The duration of the sampling was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Hazard quotients for concentrations of TMX in bee-relevant matrices from wOSR grown from seeds treated with TMX near Vingre, Picardie, France (data from Report RJ37748 Tables 3 and 4 and from Report CEMS-2898 Tables 2 - 5)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
wOSR grown from treated seed.	max. in pollen collected by bees (n = 27)	1.0	0.1	8.6	Larva	124
wOSR grown from treated seed.	max. in nectar collected by bees (n = 26)	1.4	0.4	8.6	Adult	292
wOSR grown from treated seed.	max. in wax from hive (n = 79)	0.0	NA	8.6	NA	NA
wOSR grown from treated seed.	max. in pollen from hive (n = 54)	1.0	0.12	8.6	Larva	124
wOSR grown from treated seed.	max. in nectar from hive (n = 78)	0.0	0.0	8.6	Adult	292
wOSR grown from treated seed.	max. in honey from hive (n = 16)	0.0	0.0	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in wax in the hive resulted in exposures that were assumed to be less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.	**0**

Response 4: Relevance to adverse effects			Score
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in honey in the hive collected by bees resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 24, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2010l)
Report: Syngenta. 2010. Thiamethoxam - A Semi-field Study with Maize Seeds Treated with A9700B and A14304E, Investigating Residues in Guttation Liquid in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10918 - A9700B, A14304E (S09-02828). 77 p.

The purpose of the study is to determine, under semi-field conditions, the concentration of TMX and the metabolite clothianidin in guttation liquid of maize plants grown from seeds treated with two different seed treatments, each containing TMX.

Responses 1-2: Quality of methods			**Score**
Experimental design and hypotheses	The study was conducted in the Letnitza region of Bulgaria in 2009. Maize seeds (*Zea mays*; var. Amadeo) were treated with A9700B: TMX at 0.64 mg/seed or with A14304E (TMX at 0.27 mg/seed and Tefluthrin; rate of TMX measured). The two treatments were replicated four times and the control had only one replicate. Each plot was covered by a single tunnel and plots were ca. 19.4 m^2. The single control was 9.72 m^2. Seeds were sown on 2009-09-05 and the plots were fitted with drip irrigation. Plants emerged on 2009-09-14. Weather data for the trial period were taken from the nearby official weather station (non-GLP). Samples of soil were taken to characterize properties. When guttation was observed, the guttation droplets were collected from the leaf edge with 200 µL glass capillary tubes and pooled in Eppendorf tubes. Samples were taken from a minimum of 12 different points distributed over the replicate plot. Guttation fluid was sampled on 3, 7, 10, 14, 17, 21, 24, 28, 31, 35, 38, 42, 45 and 49 d after emergence. Treated and control samples were kept separate and were stored at (≤-18C). Analyses were conducted using a standard method for LC-MS/MS. The LOQ was 0.05 µg/L. Isotopically labeled internal standards were not used but standards were >98% pure. Percent recovery(%RSD) was 92(7%) and 90(13%) for TMX and clothianidin, respectively. Graphs of mean concentrations in the treatments showed rapid dissipation of the residues of TMX and the metabolite clothianidin. Residues of TMX and clothianidin were above the LOD in the controls on d 3 of sampling (*weakness*).		**3**
Use of GLP and QA/QC	GLP study with QA and QC.		**4**
Transparency of data	All raw data were provided but only means were calculated.		**4**
Number of samples and replication	One site for each treatment and with four replicate subplots for each treatment and one replicate subplot for the control.		**2**
Duration of study sufficient to observe trends	The duration of the study (49 d) was appropriate to the objectives.		**4**
Overall evaluation of methods	Computed mean of above		**3.4**
Score for expert judgment on Quality of the study.		**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX guttation fluid from maize grown from seeds treated with TMX in Bulgaria (data from p 24-27)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize treated with 0.64 mg TMX/seed	Guttation fluid median (n = 56)	108	0.86	8.6	Adult	8
Maize treated with 0.64 mg TMX/seed	Guttation fluid 90th centile (n = 56)	1421	11.37	8.6	Adult	8
Maize treated with 0.27 mg TMX/seed	Guttation fluid median (n = 56)	37	0.30	8.6	Adult	8
Maize treated with 0.27 mg TMX/seed	Guttation fluid 90th centile (n = 56)	696	5.57	8.6	Adult	8

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile but not the median concentration of ΣTMX measured in guttation fluid from maize treated with 0.64 mg TMX/seed was greater than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile and the median concentration of ΣTMX measured in guttation fluid from maize treated with 0.27 mg TMX/seed was less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2010k)
Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Semi-Field Study with A9700B + A9638A Treated Maize Seed, followed by Untreated Flowering Crop(s), Investigating Residues in Crop(s), Soil and Honeybee Products in Picardie (France), in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10914 - A9700B. 184 p

The objective of the study was to determine the magnitude of residues of TMX and its metabolite clothianidin in crop, soil and honeybee products in flowering crops grown in fields the season after the use of TMX as a seed treatment for maize and barley.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	Maize (var. Nebora) pre-treated with the seed treatment TMX + A9638A was sown (target seed rate – 28 kg/ha) in a field plot near Appilly in the region Picardie, France in spring 2008 (Tables 2 and 4). Based on analysis, the rate of TMX applied was 76.80 g/ha. The maize planting occurred in the spring (May 3 2008). Seeding was with Monosem drill. This followed by a seeding of winter barley (var. Esterel) treated with TMX sown in the same field plot in autumn 2008 (12 November 2008) with an Amazone 4M drill. The rate of TMX applied with the seed dressing was 71.78 g/ha (analysed). The treated field plots were matched with a similar size control field plot sown with untreated seeds. Weather conditions during the entire study were recorded (Tables 27 & 28; Figures 9 and 10). No products containing neonicotinoids were applied during the study period; historical pesticide use was known and no neonicotinoid insecticides or seed treatments were used in the field plots in at least the previous cropping season before use. In 2009 soil was sampled, characterized and chemically analysed for TMX residues, and then the control and the treated field plots were split into four parts in spring 2009 (Figure 2) and separated by a buffer zone. The parts were large enough to accommodate 3 tunnels (size of 5 m x 40 m) with at least 2 m distance between each tunnel. Three different untreated flowering crops were used in 2009: summer oilseed rape (sOSR - var. Ability), *Phacelia tanacetifolia* (var Angelia) and alfalfa (var. Marshal). The first seeding of each crop always was in the control field. sOSR was drilled on March 20 and April 2, 2009; alfalfa drilled on April 2, 2009, and *Phacelia* on May 20, 2009. Two parts were planted with sOSR, 1 with alfalfa and 1 with *Phacelia*. Seedling rates and methods including calibration of drilling machines were provided and followed good agricultural practices. Prior to the onset of flowering, three tunnels were set-up on each flowering crop in the TMX-treatment field plots and one tunnel on each flowering crop in the control field plots. One bee colony (one queen, two brood bodies,10-20 combs, certified healthy) was placed in each tunnel during the flowering phase (Figure 3). For the control plots, there was only one tunnel with one hive. Forager bees were collected on three sampling days approximately 1, 3 and 7 days after initial exposure to flowering crops. Samples were collected between June 8 and July 20, 2009. Appropriate precautions to avoid cross contamination were used for all sampling. On each sampling day, three samples of approximately 300 forager bees containing approximately 150 bees with pollen loads were taken per tunnel. Forager bees were collected as they returned to the	**4**

Responses 1-6: Quality of methods		Score
	hive by suction or by brushing them into a box filled with dry ice or by using a pair of tweezers. After each sampling interval, the hive was re-opened. After the sampling, each sample was divided into two sub-samples (A and B), each with approximately 150 bees, one for preparation and one as a retained sample (B). To avoid damage during storage and shipment bees were transferred and transported in polyethylene bottles. Samples were chilled using dry ice during transport (-1.0 to +12°C) to the freezer and were subsequently stored deep frozen ≤-18°C. Bees were then shipped frozen to LAVES bee institute in Celle, Germany for preparation of the honey stomachs and pollen loads. The honey stomachs were removed after the bees had thawed for a few minutes. Bees were held by the thorax and their abdomens stretched flat with forceps. The abdomens or the tergite plates were pulled off to free the honey stomach. The front part of the oesophagus was removed by pulling it off, the honey stomach transferred onto a tarred slide, and weighed. The contents of the honey stomachs from one sampling time, treatment, and replicate were pooled to get at least 0.2 g per sample. Bees from the control were processed first then the bees for the treatments. For the preparation of pollen from the forager bees, the pollen loads were detached from the legs of the thawed forager bees and placed into a vial. For nectar and pollen, if there was <0.1 g in the A sub-sample available then the B sub-sample was prepared and added to the A sub-sample to produce one sample for analysis. If the weight of A and B samples together was still below 0.1 g additional samples were pooled for analysis the following sequence was followed. First the specimens from one tunnel were pooled. If the weight was still too low for analytical analysis specimens from a whole sampling day were pooled and if still too low for analysis, samples from the entire crop were used in the analysis. After preparation, the contents of the honey stomachs and the pollen were stored separately and deep frozen ≤-18°C. Samples were shipped on dry ice to the CEMAS, North Ascot, UK for analysis. Analysis followed standard methods and was by LC-MS/MS. Isotopically labeled internal standards were not used but standards for TMX and clothianidin were 99.7 and 98% pure. The LOQs for TMX and clothianidin in pollen from sOSR, *Phacelia*, and Alfalfa were 1 µg/kg. The LOQs for TMX and clothianidin in nectar from sOSR, *Phacelia*, and Alfalfa were 0.5 and 1 µg/kg, respectively. Recoveries (RSDs not provided) for TMX in pollen from sOSR, *Phacelia*, and alfalfa were 109, 94, and 89%, respectively. For clothianidin, they were 97, 98, and 90%, respectively. Recoveries (RSDs not provided) for TMX and in nectar from sOSR, *Phacelia*, and alfalfa were 90, 78, and 100%, respectively. For clothianidin, they were 95, 86, and 99%, respectively (Appendix 7, Tables 11-16). Neither TMX nor clothianidin were detected in the control samples.	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures and etc.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site with one control field and three subfields each with three tunnels for each follow-on crop.	**2**

Responses 1-6: Quality of methods			Score
Duration of study sufficient to observe trends	There were three samples taken during the exposure period when plants were flowering. This is appropriate for the design of the study.		**4**
Overall evaluation of methods			**3.60**
Score for expert judgment on quality of the study		**1**	**3.60**

Relevance

Hazard quotients for concentrations of ΣTMX in nectar and pollen from sOSR, *Phacelia*, and alfalfa grown in fields the season after the use of TMX as a seed treatment for maize and barley in Picardie, France (data from Appendix 7, Tables 1-6).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
sOSR as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, 90th centile (n = 36)	10.3	1.28	8.6	Larva	124
sOSR as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 33)	3	0.88	8.6	Adult	292
Phacelia as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, 90th centile (n = 20)	4.5	0.56	8.6	Larva	124
Phacelia as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 36)	0.95	0.28	8.6	Adult	292
Alfalfa as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, max. (n = 2)	0	0.00	8.6	Larva	124
Alfalfa as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 36)	0	0.00	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from sOSR as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from sOSR as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from *Phacelia* as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from *Phacelia* as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from alfalfa as a follow-on crop to maize and barley seed-treated with TMX resulted in a maximum exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from alfalfa as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2010j)
Report: Syngenta. 2010c. Thiamethoxam (CGA293343) - A Semi-Field Study with A9700B + A9638A Treated Maize Seed, Followed by Untreated Flowering Crop(s), Investigating Residues in Crop(s), Soil and Honeybee Products in Alsace (France), in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10915 - A9700B. 184 p

The objective of the study was to determine the magnitude of residues of TMX and its metabolite clothianidin in crop, soil and honeybee products in flowering crops grown in fields the season after the use of thiamethoxam as a seed treatment for maize and barley.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	Maize (var. Nebora) pre-treated with the seed treatment TMX + A9638A was sown (target seed rate- 28 kg/ha) with a Monosem drill in a field plot near Drusenheim in the Alsace region of France (Tables 2 and 4) in spring 2008 (April 28, 2008). TMX application was nominal 220.5 g TMX per 100 kg seed (actual measured at 287 g/100 kg seed). The maize was followed by a seeding of winter barley (var. Esterel) treated with TMX only sown (target seeding rate- 110 kg/ha; Table 5)) in the same field plot in autumn (September 29, 2008) with a Sulky drill. The nominal rate of TMX applied with the seed dressing was at approximately 70 g TMX/100 kg seed (actual analysed 66.4 g/100 kg seed; Table 3). Meteorological data were provided (Tables 27 and 28; Figures 9 and 10). No products containing neonicotinoids were applied during the study period; historical pesticide use was known and no neonicotinoid insecticides or seed treatments were used in the field plots in at least the previous cropping season before use. This was confirmed by residue analysis of the soil taken before application. Loading and drilling rates were verified (Tables 8 and 9 for maize; Tables 11 and 12 for winter barley). Soils were characterized and chemically analysed for TMX residues. The treated field plots were matched with a similar size control field plot sown on with untreated seed (Tables 8, 11, 14, 17, 20 and 23). In spring 2009, the fields (TMX and control fields) were divided into four parts (Figure 2) and planted with untreated flowering crops (alfalfa – var. Marshal; summer oilseed rape (sOSR) - var. Ability) and *Phacelia tanacetifolia* – var. Angelia) on April 3, 2009, March 23 and April 3, 2009, and May 4, 2009, respectively. Two parts were planted with sOSR, 1 with alfalfa and 1 with *Phacelia*. Seedling rates and methods including calibration of drilling machines were provided and followed good agricultural practices. Prior to the onset of flowering, three tunnels were set-up on each flowering crop in the TMX-treatment field plots and one tunnel on each flowering crop in the control field plots. One bee colony (one queen, two brood bodies, 10-20 combs, certified healthy) was placed in each tunnel during the flowering phase (Figures 3-5). For the control plots, there was only one tunnel with one hive. Forager bees were collected on three sampling days approximately 1, 3 and 7 days after initial exposure to flowering crops. Samples were collected between June 12 and July 22, 2009. Appropriate precautions to avoid cross contamination were used for all sampling. On each sampling day, three samples of approximately 300 forager bees containing approximately 150 bees with pollen loads were taken per tunnel. Forager bees were collected as they returned to the	**3**

Responses 1-6: Quality of methods		Score
	hive by suction or by brushing them into a box filled with dry ice or by using a pair of tweezers. After each sampling interval, the hive was re-opened. After the sampling, each sample was divided into two sub-samples (A and B), each with approximately 150 bees, one for preparation and one as a retained sample (B). To avoid damage during storage and shipment bees were transferred and transported in polyethylene bottles. Samples were chilled using dry ice during transport (-36.0 to +0.5°C) to the freezer and were subsequently stored deep frozen ≤-18°C. Bees were then shipped frozen to LAVES bee institute in Celle, Germany for preparation of the honey stomachs and pollen loads. The honey stomachs were removed after the bees had thawed for a few minutes. Bees were held by the thorax and their abdomens stretched flat with forceps. The abdomens or the tergite plates were pulled off to free the honey stomach. The front part of the oesophagus was removed by pulling it off, the honey stomach transferred onto a tarred slide, and weighed. The contents of the honey stomachs from one sampling time, treatment, and replicate were pooled to get at least 0.2 g per sample. Bees from the control were processed first then the bees for the treatments. For the preparation of pollen from the forager bees, the pollen loads were detached from the legs of the thawed forager bees and placed into a vial. For nectar and pollen, if there was <0.1 g in the A sub-sample available then the B sub-sample was prepared and added to the A sub-sample to produce one sample for analysis. If the weight of A and B samples together was still below 0.1 g additional samples were pooled for analysis the following sequence was followed. First the specimens from one tunnel were pooled. If the weight was still too low for analytical analysis specimens from a whole sampling day were pooled and if still too low for analysis, samples from the entire crop were used in the analysis. After preparation, the contents of the honey stomachs and the pollen were stored separately and deep frozen ≤ -18°C. Samples were shipped on dry ice to the CEMAS, North Ascot, UK for analysis. Analysis followed standard methods and was by LC-MS/MS. Isotopically labeled internal standards were not used but standards for TMX and clothianidin were 99.7 and 98% pure. The LOQs for TMX and clothianidin in pollen from sOSR, *Phacelia*, and Alfalfa were 1 µg/kg. The LOQs for TMX and clothianidin in nectar from sOSR, *Phacelia*, and Alfalfa were 0.5 and 1 µg/kg, respectively. Recoveries (RSDs not provided) for TMX in pollen from sOSR, *Phacelia*, and alfalfa were 105, 100, and 89%, respectively. For clothianidin, they were 107, 100, and 90%, respectively. Recoveries (RSDs not provided) for TMX and in nectar from sOSR, *Phacelia*, and alfalfa were NA, 100, and 100%, respectively. For clothianidin, they were 93, 99, and 102%, respectively (Appendix 7, Tables 11-16). Neither TMX nor clothianidin were detected in the control samples except one *Phacelia* pollen sample where residues of TMX and CTD were detected (*weakness*). This was attributed to most likely contamination during preparation of the sample.	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures, and etc.	**4**
Transparency of data	All raw data were provided.	**4**

Responses 1-6: Quality of methods			Score
Number of samples and replication	There was one site with one control field and three subfields each with three tunnels for each follow-on crop.		**2**
Duration of study sufficient to observe trends	There were three samples taken during the exposure period when plants were flowering. This is appropriate for the design of the study.		**4**
Overall evaluation of methods			**3.40**
Score for expert judgment on quality of the study		**1**	**3.40**

Relevance

Hazard quotients for concentrations of ΣTMX in nectar and pollen from sOSR, *Phacelia*, and alfalfa grown in fields the season after the use of TMX as a seed treatment for maize and barley in Alsace, France (data from Appendix 7, Tables 1-6).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
sOSR as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, 90th centile (n = 29)	2.5	0.31	8.6	Larva	124
sOSR as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 24)	1.3	0.38	8.6	Adult	292
Phacelia as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, 90th centile (n = 32)	7.6	0.94	8.6	Larva	124
Phacelia as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 36)	0	0.00	8.6	Adult	292
Alfalfa as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, max. (n = 1)	53.3	6.61	8.6	Larva	124
Alfalfa as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 36)	0	0.00	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from sOSR as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from sOSR as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.	**0**

Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from *Phacelia* as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from *Phacelia* as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from alfalfa as a follow-on crop to maize and barley seed-treated with TMX resulted in a maximum exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from alfalfa as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2010b)
Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Semi-Field Study with A9700B + A9638A Treated Maize Seed, followed by Untreated Flowering Crop(s), Investigating Residues in Crop(s), Soil and Honeybee Products in Burgundy (France), in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10916 - A9700B. 154 p

The objective of the study was to determine the magnitude of residues of TMX and its metabolite clothianidin in crop, soil and honeybee products in flowering crops grown in fields the season after the use of thiamethoxam as a seed treatment for maize and barley.

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	Maize (var. Nebora) pre-treated with the seed treatment TMX + A9638A was sown (nominal and actual target seed rates- 28 and 20.9 kg/ha) with a Monosem drill in a field plot near Saint Cyr in the Burgundy region of France (Tables 2 and 4) in spring 2008 (May 15, 2008). TMX application was nominal 220.5g TMX per 100 kg seed (actual measured 287 g/100 kg seed). The maize was followed by a seeding of winter barley (var. Esterel) treated with TMX only sown (target seeding rate- 110 kg/ha; Table 5) with an unspecified drill in the same field plot in autumn (November 27, 2008). The nominal rate of TMX applied with the seed dressing was at approximately 70 g TMX/100 kg seed (actual measured 66.4 g/100 kg seed; Table 3). The treated field plots were matched with a similar size control field plot sown (maize – 24.05 kg/ha; barley – 116.5 kg/ha) with untreated seed (Tables 8 and 11). The seeding rates for subsequent plant crops were provided in Tables 14, 16, 18 and 20. No products containing neonicotinoids were applied during the study period; historical pesticide use was known and no neonicotinoid insecticides or seed treatments were used in the field plots in at least the previous cropping season before use. This was confirmed by residue analysis of the soil taken before application. Loading and drilling rates were verified (Tables 8 and 9 for maize; Tables 11 and 12 for winter barley). Meteorological data were recorded (Tables 24 and 25; Figures 9 and 10). Soils were characterized and chemically analysed for TMX residues. In spring 2009, the fields (TMX and control fields) were divided into four parts (Figure 2) and planted with untreated flowering crops (alfalfa – var. Marshal; summer oilseed rape (sOSR) - var. Ability) and *Phacelia tanacetifolia* – var. Angelia) on April 6, 2009, March 25 and April 6, 2009, and May 12, 2009, respectively. Two parts were planted with sOSR, 1 with alfalfa and 1 with *Phacelia*. Seedling rates and methods including calibration of drilling machines were provided and followed good agricultural practices. Prior to the onset of flowering, four tunnels were set-up on each flowering crop in the treated field plot and one tunnel on each flowering crop in the control field plot (Figure 3-5). In each tunnel one bee colony (one queen, two brood bodies,10-20 combs, certified healthy) was placed during the flowering phase (~7 days). Because of damage inflicted by pollen beetle in the tunnels, sOSR was removed from the study. Forager bees were collected on three sampling days approximately 1, 3 and 7 days after initial exposure to flowering crops. Samples were collected between July 10 and July 20, 2009.	**4**

Responses 1-3: Quality of methods		Score
	Appropriate precautions to avoid cross contamination were used for all sampling. On each sampling day, three samples of approximately 300 forager bees containing approximately 150 bees with pollen loads were taken per tunnel. Forager bees were collected as they returned to the hive by suction or by brushing them into a box filled with dry ice or by using a pair of tweezers. After each sampling interval, the hive was re-opened. After sampling, each sample was divided into two sub-samples (A and B), each with approximately 150 bees, one for preparation and one as a retained sample (B). To avoid damage during storage and shipment bees were transferred and transported in polyethylene bottles. Samples were chilled using dry ice during transport (-41.5 to +8.4°C) to the freezer and were subsequently stored deep frozen ≤-18°C. Bees were then shipped frozen to LAVES bee institute in Celle, Germany for preparation of the honey stomachs and pollen loads. The honey stomachs were removed after the bees had thawed for a few minutes. Bees were held by the thorax and their abdomens stretched flat with forceps. The abdomens or the tergite plates were pulled off to free the honey stomach. The front part of the oesophagus was removed by pulling it off, the honey stomach transferred onto a tarred slide, and weighed. The contents of the honey stomachs from one sampling time, treatment, and replicate were pooled to get at least 0.2 g per sample. Bees from the control were processed first then the bees for the treatments. For the preparation of pollen from the forager bees, the pollen loads were detached from the legs of the thawed forager bees and placed into a vial. For nectar and pollen, if there was <0.1 g in the A sub-sample available then the B sub-sample was prepared and added to the A sub-sample to produce one sample for analysis. If the weight of A and B samples together was still below 0.1 g additional samples were pooled for analysis the following sequence was followed. First the specimens from one tunnel were pooled. If the weight was still too low for analytical analysis specimens from a whole sampling day were pooled and if still too low for analysis, samples from the entire crop were used in the analysis. After preparation, the contents of the honey stomachs and the pollen were stored separately and deep frozen ≤ -18°C. Samples were shipped on dry ice to the CEMAS, North Ascot, UK for analysis. The amount of pollen collected from alfalfa was too small for analysis. Analysis followed standard methods and was by LC-MS/MS. Isotopically labeled internal standards were not used but standards for TMX and clothianidin were 99.7 and 98% pure. The LOQs for TMX and clothianidin in pollen from sOSR, *Phacelia*, and Alfalfa were 1 µg/kg. The LOQs for TMX and clothianidin in nectar from sOSR, *Phacelia*, and Alfalfa were 0.5 and 1 µg/kg, respectively. Recovery (RSDs not provided) for TMX in pollen from *Phacelia* was 99%. For clothianidin, recovery was 102%. Recoveries (RSDs not provided) for TMX and in nectar from *Phacelia* and alfalfa were 107, and 103%, respectively. For clothianidin, they were 103 and 85%, respectively (Appendix 7, Tables 8-10). Neither TMX nor clothianidin were detected in the control samples.	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures and etc.	**4**
Transparency of data	All raw data were provided.	**4**

Responses 1-3: Quality of methods			Score
Number of samples and replication	There was one site with one control field and three subfields each with three tunnels for each follow-on crop.		**2**
Duration of study sufficient to observe trends	There were three samples taken during the exposure period when plants were flowering. This is appropriate for the design of the study.		**4**
Overall evaluation of methods			**3.60**
Score for expert judgment on quality of the study		**1**	**3.60**

Relevance

Hazard quotients for concentrations of ΣTMX in nectar and pollen from sOSR, *Phacelia*, and alfalfa grown in fields the season after the use of TMX as a seed treatment for maize and barley in Burgundy, France (data from Tables 36-38).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Phacelia as a follow-on crop to maize and barley seed-treated with TMX	Pollen from bees, 90th centile (n = 34)	2.3	0.29	8.6	Larva	124
Phacelia as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 36)	0	0.00	8.6	Adult	292
Alfalfa as a follow-on crop to maize and barley seed-treated with TMX	Nectar from bees, 90th centile (n = 25)	0	0.00	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from *Phacelia* as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from *Phacelia* as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar from alfalfa as a follow-on crop to maize and barley seed-treated with TMX resulted in a 90th centile exposure <NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**

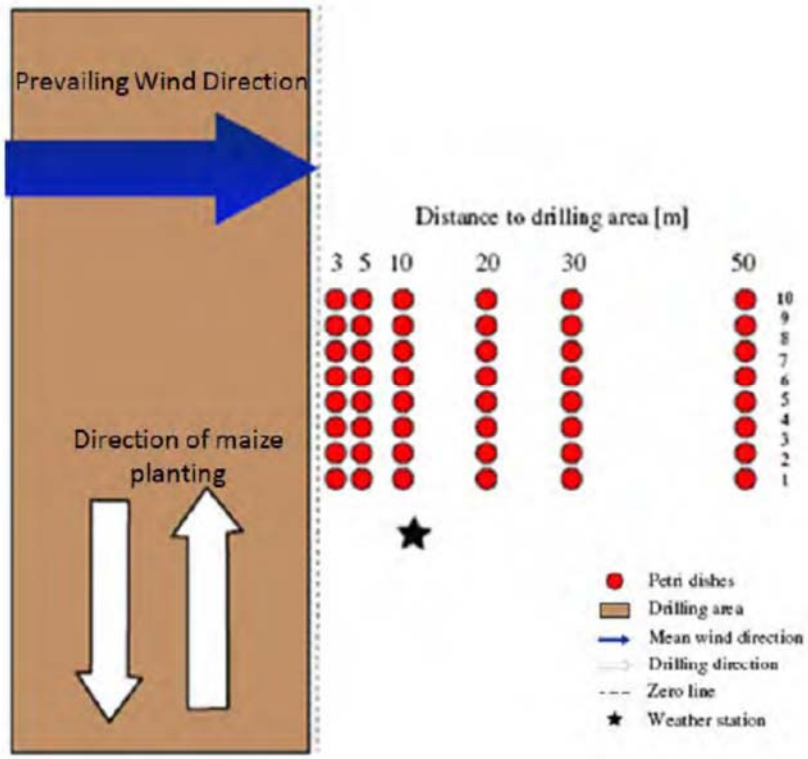
Score for expert judgment on relevance of the results.	**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2010i)
Report: Syngenta. 2010. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Seeding and Residues in Guttation Liquid, on Honeybee Colonies in Alsace (France) in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10921 - A9700B. 230 p.

The objective of the study was to determine the effect of residues of thiamethoxam and clothianidin in dust generated during maize seeding and residues in guttation liquid on honeybee colonies under field conditions. Only the concentrations of TMX in deposition collectors, guttation fluid, nectar and pollen from OSR were assessed in this WoE.

Responses 1- 4: Quality of methods		**Score**
Experimental design and hypotheses	The study was well described but too many different matrices were sampled and none, except guttation fluid, was well done (*weakness*). The study was carried out at two separate field plots (approximately 1.8 ha in the control and 1.4 ha in the TMX treated field plot; separated by 2.5 km) located near Drusenheim in the region of Alsace, France. On both field plots, maize seed (var. Zorrero) treated with Cruiser 350 FS / Influx XL 035FS (fludioxonil) was drilled (Monosem seeder) at approximately 110,000 seeds/ha (target 69.3 g TMX/ha in the treated plot; actual was 78.7 g TMX/ ha; 0.70 mg TMX/seed). The control (TMX-free seed) and TMX-treated seed were drilled on May 5 and 6, 2009, respectively (Tables 5 and 6). Application rates were verified and the loading rates and drill rates summarized on p. 21 (Tables 5 and 6). Six bee colonies were placed at the treated and six at the control field plots. The adjacent crop was winter oilseed rape (wOSR) from which dust samples were collected and observations on foraging honeybees were made. Meteorological data were recorded (Tables 5–9). Historical pesticide use was reported (Tables 1 and 2, respectively) for both the TMX and control fields. Soils were characterized (Subsection 4.1, p. 26) and although soil samples were collected, no residues were measured (p. 20). Honeybee colonies (n = 6 hives/treatment; healthy queen-right) were placed into the maize field plots (Figures 2 and 3) comprising the TMX and control treatments on April 24, 2009 just before maize seeding and were maintained from seeding for up to 41 days after maize emergence (exposure phase). In the treated field, colonies were positioned within the oilseed rape crop with the hive entrances facing the oilseed rape crop (Figure 4). In the control field, hives were positioned on the grass verge at the edge of the field, all facing toward the oilseed rape crop (Figure 5). Afterwards the bee colonies were moved on 23 June 2009 and maintained and observed at a monitoring site (Wissembourg), without extensive agricultural crops attractive to bees. Sampling of deposition of dust: Six rows of five Petri-dishes (143.14 cm^2) were set up in the centre of the maize field in a corridor cleared in the OSR field, downwind of the test plot at distances of 3, 5, 10, 20, 30, and 50 m from the zero line of the first pass (see diagram below). Dishes were also set up in the OSR crop on ground level and at the height of the canopy. Each dish contained 50 mL of a 1:1 solution of glycerol and ultra-pure water. Samples were covered with lids and collected after drilling. After deposition, samples were transferred to	**3**

Responses 1- 4: Quality of methods		Score
	250-mL polypropylene bottles with the aid of rinses of ultrapure water. Of the 6 distances set-up at the three positions in the oilseed rape the 3 m and 5 m were analyzed because of unfavorable wind conditions during application. Flower heads of OSR downwind from the test field were also sampled but were not included in the WoE. Field recovery samples were placed in an up-wind area of the test plot, six Petri dishes, filled with glycerol/deionized water (50:50 v/v) as trapping solution (50 mL) were set-up. The Petri dishes were spiked with TMX at three concentrations with a hand-held Eppendorf dispenser.  Sampling of nectar and pollen from bees took place 2 and 7 d after seeding but only the d-7 samples were analyzed. Forager bee samples were collected in the first sampling (3 days after seeding) from one hive in both treatment plots and in the second sampling (7 days after seeding) from five hives in the treatment and from all six hives in the control. One sample of 300 forager bees was taken on each sampling occasion. The pollen samples were stored in separate containers, sealed and uniquely labelled. The samples were transported on dry ice to the testing facility and were deep frozen (≤-18°C) within 12 h after sampling. The samples were shipped to the Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit (LAVES) in Celle, Germany for the honey stomach and pollen preparation. Preparation of the pollen and nectar samples was not described but was assumed to be similar to other studies by the same contractor (*potential weakness*). Residue sampling of guttation fluid was conducted at intervals during the 40-d observation period after maize emergence. When guttation was	

Responses 1- 4: Quality of methods		Score
	observed, the droplets were collected from the leaf edge with syringes or Pasteur pipettes. Guttation fluid was sampled on 1, 2, 4, 10, 16, 32 and 40 days after emergence of maize. After each sampling, the samples were stored on dry ice (cooled) during the transport to the testing facility and deep frozen (≤ -18°C) afterwards at the testing facility (within 12 h of sampling). Samples were sent to Eurofins-ADME for analysis of residues of TMX and clothianidin. Field recovery samples were treated in the same way. Analytical methods followed standard procedures and were described in detail (Appendix 4). Analysis was by LC-MS/MS. Isotopically labelled internal standards were not used but the reference standard was 99.5% pure. The LOQ for dust was 1 ng per dish. Mean recoveries(RSD) of TMX and clothianidin for dust samples were 92(7.2%) and 89(7.1%) respectively. The LOQ for pollen was 1 µg/kg and mean recoveries (no RSD) of TMX and clothianidin were 104 and 98%, respectively. The LOQ for nectar was 1 µg/kg and mean recoveries (no RSD) of TMX and clothianidin were 99 and 100%, respectively. The LOQ for guttation fluid was 0.05 µg/kg and mean recoveries (no RSD) of TMX and clothianidin were 92 and 91%, respectively. The recoveries for the field-spike samples ranged from 70 to 76% for TMX and 71-75% for clothianidin. Clothianidin was not detected in the OSR pollen and nectar samples. One control sample of guttation fluid contained TMX and clothianidin >LOQ. Concentrations of TMX in guttation fluid collected from maize declined rapidly from a high of 27,728 µg/L on May 14 to 9,779 µg/L the following day and 28 µg/L on June 22 (Table 24).	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures, etc. Meteorological data was non-GLP.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There was one site with one control and one test field. One sample of pollen and nectar from bees was analysed. Seven samples of guttation fluid were analysed.	**1**
Duration of study sufficient to observe trends	The duration of the study for the purposes of assessing guttation fluid was appropriate (2009-05-14 to 2009-06-22), but that from matrices in OSR was not.	**2**
Overall evaluation of methods		**2.80**
Score for expert judgment on quality of the study.	**1**	**2.80**

Relevance

Hazard quotients for concentrations of ΣTMX in guttation fluid from maize plants treated with TMX and grown in Alsace, France and TXM in pollen and nectar of OSR in a filed down-wind (data from Tables 21, 22, & 24).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize plants grown from seeds treated with TMX	Guttation fluid, max. (n = 7)	29899	239	8.6	Adult	8

Hazard quotients for concentrations of ΣTMX in guttation fluid from maize plants treated with TMX and grown in Alsace, France and TXM in pollen and nectar of OSR in a filed down-wind (data from Tables 21, 22, & 24).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
OSR downwind of maize plants grown from seeds treated with TMX	Pollen from bees (n = 1)	4	0.50	8.6	Larva	124
OSR downwind of maize plants grown from seeds treated with TMX	Nectar from bees (n = 1)	2	0.58	8.6	Adult	292

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Deposition of TMX at various distances away from the seeding operation with maize seeds treated with TMX in Alsace France (Table 18).

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Collectors on bare ground	max. deposition 3 m (n = 10)	0.0155	0.16	0.1
Collectors on ground under OSR	max. deposition 5 m (n = 10)	0.0030	0.03	0.1
Collectors at height of OSR canopy	max. deposition 3 m (n = 10)	0.0061	0.06	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of ΣTMX measured in guttation fluid resulted in exposures that were >NOAED for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected by bees from OSR resulted in exposures that were >NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected by bees from OSR resulted in exposures that were <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	Maximum mean deposition of TMX dust measured in collectors on bare ground were <NOAER.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	Maximum mean deposition of TMX dust measured in collectors on ground under the OSR crop were <NOAER.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	Maximum mean deposition of TMX dust measured in collectors at the canopy height of OSR were <NOAER.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2011b)
Report: Syngenta. 2011. Determination of Residues of Thiamethoxam and its Metabolites in Sweet Corn and Sorghum Pollen after Drilling of Seeds Treated with A9700B, France 2010. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10940 - A9700B (S10-01907). 130 p

The objective of the study was to determine the concentration of TMX and its metabolite clothianidin in pollen, following planting and cultivation of sweet corn and sorghum seeds treated with TMX.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	This study was undertaken at three locations in France with *Zea mays* (var. Bonus) and *Sorghum vulgare* (var. Arakan) in 2010. Plots were small (< 1 ha; 30 m^2 – 120 m^2). Seeds were treated with Cruiser 350 FS at measured rates of 0.57 and 0.101 mg TMX/seed, respectively. The historical use of crops and pesticides at each site was reported (Table 4-9) and pesticides used during the study was documented (Table 10). No nicotinoids were used prior to or during the trials. Fertilizer use and irrigation were documented (Tables 11-12) and weather conditions were reported (Tables 13-15). Distance between control plot and treatment plot was at least 60 m for all trials. Sowing date varied by location and was carried out on 2010-05-19, 2010-05-25, 2010-06-01, and 2010-06-02. Pollen was sampled directly from the plants. All inflorescences used for pollen sampling were covered with water-proof paper bags before the start of flowering. In the control plots, at least 50 tassels (for sweet corn and sorghum) split over at least 12 different locations were covered. In the treated plots, at least 150 tassels in maize and 300 inflorescences in sorghum; split over at least 12 different locations were covered. The bags were placed vertically on the inflorescence and tied with clips. Pollen samples were collected at BBCH stages 63-64 and 65-67. For sweet corn, the male flower was cut off. The bag with the male flower inside was shaken for a few seconds to break the anthers. For sorghum, the whole inflorescence was cut off. The bag was shaken for a few seconds, resulting in pollen being shed into the bag. After removing the bags from the plants, pollen in the bags from each plot were pooled. If necessary, the pooled sample was sieved with a fine tea strainer (unreported mesh size (*potential weakness*)) to clean up the pollen. The control sample was always taken first followed by the treated sample. Samples were frozen at ≤-18C during storage and shipment for analysis (Tables 22-27). Analysis was conducted at Eurofins ADME BIOANALYSES using a standard method (REM179.07). Isotopically labeled internal standards were not used but standards for TMX and clothianidin were >98% pure. The LOQ was 1 µg/kg. Recover for TMX and clothianidin in maize were 89 and 92%, respectively. For sorghum, recovery(%RSD) were 93(13%) and 86(10%), respectively. TMX and clothianidin were not detected in the controls or in any of the treated plots.	**4**
Use of GLP and QA/QC	GLP study with QA and QC.	**4**
Transparency of data	All raw data were provided but only means were calculated.	**4**

Responses 1-2: Quality of methods			Score
Number of samples and replication	There were three sites for each treatment and one replicate subplot per test species.		**2**
Duration of study sufficient to observe trends	The duration of the study (49 d) was appropriate to the objectives.		**4**
Overall evaluation of methods	Computed mean of above		**3.6**
Score for expert judgment on Quality of the study.		**1**	**3.60**

Relevance

Hazard quotients for concentrations of TMX in pollen from maize and sorghum grown from seeds treated with TMX in three locations in France (data from Tables 28-32).

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize treated with 0.63 mg TMX/seed	Pollen from plants max. (n = 18)	0	0.00	8.6	Larva	124
Sorghum treated with 0.107 mg TMX/seed	Pollen from plants max. (n = 10)	0	0.00	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from maize plants grown from treated seed in France resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen collected from sorghum plants grown from treated seed in France resulted in exposures that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2012d)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Stade, Germany in 2010. Final Report Amendment 1. Syngenta Ltd, Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). No. A9700B-S10-01860. 366 p

The focus of this report was on the effects of dust from planting of maize seeds treated with TMX on honey-bees. This was a field study, which included the collection and analysis of guttation fluid from young maize plants and in pollen from maize plants and collected by forager bees, in soil, and in maize plants. The data for guttation fluids and pollen are the focus of this WoE.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in region of Niedersachsen, Germany from 14 May 2010 to 29 March 2011. The study was well described. There was one treatment and one control plot. The treated plot was 1.57 ha, control was 1.53 ha (Table 40). Test and control plots were 12 km apart and were ≥1.5 km from other maize fields. Seeds of maize (var. NK Falkone) were treated with TMX (0.69 mg/seed); fludioxonil; 2.54 g/100 kg seed; and metalaxyl-M, 1.12 g/100 kg seed (measured concentrations). Seeds were sown on 18 May 2010. The treated field was sown at 111,026 seeds/ha (equivalent to 34.64 kg seeds/ha), resulting in an application rate of 76.6 g TMX/ha. The control was sown with the same var. (untreated) at 111,058 seeds/ha (34.65 kg seeds/ha). Seeding was conducted with a Becker Aeromat fitted with a deflector to direct the outlet air towards the surface of the soil. Bees were present during seeding but deposition of dust was not measured (*weakness*). The use of appropriate crop protection chemicals (no neonicotinoids) was recorded and the same chemicals were applied to the test and control fields (Tables 47 to 50). Weather conditions were recorded (Tables 24-26) Guttation was observed more frequently in the morning and number of plants showing guttation was similar in treatment and control. Guttation fluid was collected from 31 May 2010 (emergence of maize plants) and 8 July 2010 (towards the end of guttation). If guttation was observed in the test field, droplets were collected from the leaf edges with capillary micropipettes (25 µL or 200 µL) and then transferred to Eppendorf tubes. Guttation fluid was sampled daily in the first week, twice in the second week and once in each following week after emergence of maize seedlings. If possible, on each sampling day three samples of 0.5 mL were collected from a maximum of 200 plants not located within 1.5 m of the edge of the field. Samples were stored frozen (≤-18 °C) within 12 h after sampling until analysis. Guttation fluid was not sampled from the control plants *(potential weakness).* Pollen from plants and collected by bees was sampled on one day only (d-5 after flowering, 3 August 2010). The tassel of a maize plant was held in a plastic bag and shaken for a few seconds to cause pollen-shed. At least five plants at each of 12 different locations in the test and control fields were sampled. Precautions were taken to avoid	**3**

Responses 1-2: Quality of methods			Score
	contamination. Pollen from each field was pooled, chilled during transport to the freezer, and subsequently stored deep frozen at ≤-18°C until analysis. Forager bees (ca. 50 from each of the six bee-hives) were collected with a hand-vac. and directly frozen on dry ice. The subsamples were pooled, chilled during transport to the freezer and subsequently stored at ≤-18°C. Pollen loads from the forager bees were prepared at LAVES in Celle, Germany. Bees were thawed for a few minutes and the pollen loads were detached from the legs of the forager bees and placed into a vial. The pollen samples were unfrozen for <2 h during the preparation. Pollen was transferred back to the freezer immediately after preparation and stored at ≤-18°C. Conditions of storage of samples were recorded (Table 53). Samples for residue analysis were shipped frozen on dry ice to ADME, Vergènze, France for analysis. The analysis was well-described (Appendix 3). The standards for TMX and clothianidin were 99.7 and 98% pure. Isotopically labelled internal standards were not used. Analysis was by LC-MS/MS. The LOQs for TMX and clothianidin were 1 µg/kg (text) but Table 35 shows 5 µg/kg as the LOQ for pollen from bees. Recovery(RSD) of TMX and clothianidin from pollen was 86(14%) and 89(13%), respectively (Appendix 3, Table 1). For guttation fluid recovery (no RSD reported) was 94 and 96%, respectively. There was insufficient sample for analysis of pollen from bees foraging in the treated field. Pollen from the control plants contained TMX and clothianidin (261 and 36 µg/kg, respectively (***major weakness***)) but not the pollen from the bees, suggesting mix up of samples. Pollen from the treated plants had concentration <LOQ. Residues of ΣTMX in guttation fluid declined over the period of sampling. Values ranged from 28,617 µg/L on May 31 to 39 µg/L on Jul 8 (Table 37).		
Use of GLP and QA/QC	The study was GLP with full QA and QC.		**4**
Transparency of data	Raw data were provided in the report.		**4**
Number of samples and replication	There was one site and one replicate		**1**
Duration of study sufficient to observe trends	For guttation fluid, the period of sampling was appropriate. Pollen was collected on one day only.		**3**
Overall evaluation of methods	Computed mean of above		**3**
Score for expert judgment on Quality of the study. Presence of residues in the controls was identified as a **major weakness**		**0.5**	**1.50**

Relevance

Hazard quotients for concentrations of ΣTMX in pollen and guttation fluid from maize plants treated with TMX and grown in Germany (data from Tables 34 & 37).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize plants grown from seeds treated with TMX	Guttation fluid, 90th centile (n = 42)	29848	239	8.6	Adult	8
Maize plants grown from seeds treated with TMX	Pollen from plants	0	0.00	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of ΣTMX measured in guttation fluid was much greater than the NOAED for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from maize plants grown from treated seed was <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

Narrative

Residues in bees were mostly <LOQ or small for TMX but clothianidin was detected in most specimens.

(Syngenta 2012a)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (Apis mellifera L.) in Alsace, France in 2010. Final Report Amendment 1. Syngenta Ltd, Bracknell, United Kingdom: Syngenta Ltd. (Unpublished Report). No. A9700B S10-01857. 346 p.

The focus of this report was on the effects of dust from planting of maize seeds treated with TMX on honey-bees. This was a field study, which included the collection and analysis of guttation fluid from young maize plants and in pollen from maize plants and collected by forager bees, in soil, and in maize plants. The data for guttation fluids and pollen are the focus of this WoE.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in region of Alsace, France from 5 May 2010 to 21 March 2011. There was one treatment and one control plot. The treated plot was 1.97 ha and control was 2.38 ha (Table 41). Test and control plots were 4.75 km apart. Seeds of maize (var. NK Perform) were treated with TMX (0.68 mg/seed); fludioxonil 2.54 g/100 kg seed; and metalaxyl-M, 1.12 g/100 kg seed (measured concentrations). Seeds were sown on 17 May 2010. The treated field was sown at 101,684 seeds/ha (equivalent to 28.98 kg seeds/ha, resulting in an application rate of 69.15 g TMX/ha. The control was sown with the same var. (untreated) at 103,825 seeds/ha (29.59 kg seeds/ha). Seeding was conducted with a Monosem pneumatic single seed drilling machine with deflector. Bees were present during seeding but deposition of dust was not measured (*weakness*). The use of appropriate crop protection chemicals (no neonicotinoids) was recorded and the same chemicals were applied to the test and control fields (Tables 48-51). Weather conditions were recorded (Tables 26–28). Guttation was observed more frequently in the morning and number of plants showing guttation was similar in treatment and control. Guttation fluid was collected from 29 May 2010 (emergence of maize plants) to 6 July 2010 (towards the end of guttation). If guttation was observed in the test field, droplets were collected from the leaf edges with capillary micropipettes (40 µL) and then transferred to Eppendorf tubes. Guttation fluid was sampled daily in the first week, twice in the second week and once in each following week after emergence of maize seedlings. If possible, on each sampling day three samples of 0.5 mL were collected from a maximum of 200 plants not located within 1.5 m of the edge of the field. Samples were stored frozen (≤-18 °C) within 12 h after sampling until analysis. Guttation fluid was not sampled from the control plants *(potential weakness).* Pollen from plants and collected by bees was sampled on one day only (d-5 after flowering, 31 July 2010). The tassel of a maize plant was held in a plastic bag and shaken for a few seconds to cause pollen-shed. At least five plants at each of 12 different locations in the test and control fields were sampled. Precautions were taken to avoid contamination.	**2**

Responses 1-2: Quality of methods		Score
	Pollen from each field was pooled, chilled during transport to the freezer, and subsequently stored deep frozen at ≤-18°C until analysis. Forager bees (ca. 50 from each of the six hives) were collected with a hand-vac. and directly frozen on dry ice. The subsamples were pooled, chilled during transport to the freezer and subsequently stored at ≤-18°C. Pollen loads from the forager bees were prepared at LAVES in Celle, Germany. Bees were thawed for a few minutes and the pollen loads were detached from the legs of the forager bees and placed into a vial. The pollen samples were unfrozen for <2 h during the preparation. Pollen was transferred back to the freezer immediately after preparation and stored at ≤-18°C. Conditions of storage of samples were recorded (Table 55). Samples for residue analysis were shipped frozen on dry ice to ADME, Vergènze, France for analysis. The analysis was well-described (Appendix 3). The standards for TMX and clothianidin were 99.7 and 98% pure. Isotopically labelled internal standards were not used. Analysis was by LC-MS/MS. The LOQs for TMX and clothianidin were 1 µg/kg (text) but Table 35 shows 5 µg/kg as the LOQ for pollen from bees. Recovery(RSD) of TMX and clothianidin from pollen was 91(6.6%) and 88 (12.7%), resp (Appendix 3, Table 1). For guttation fluid recovery(RSD) was 91(11.4%) and 105(no RSD), respectively. There was insufficient sample for analysis of pollen from bees foraging in the treated field. Pollen from the control plants did not contain TMX or clothianidin. Pollen from the treated plants had concentration <LOQ. Residues of ΣTMX in guttation fluid declined over the period of sampling. Initial values in guttation fluid ranged from 27,829 on May 29 to 98 µg/L on July 6 (Table 39).	
Use of GLP and QA/QC	The study was GLP with full QA and QC.	**4**
Transparency of data	Raw data were provided in the report.	**4**
Number of samples and replication	There was one site and one replicate	**1**
Duration of study sufficient to observe trends	For guttation fluid, the period of sampling was appropriate. Pollen was collected on one day only.	**3**
Overall evaluation of methods	Computed mean of above	**2.8**
Score for expert judgment on Quality of the study.	**1**	**2.80**

Relevance

Hazard quotients for concentrations of ΣTMX in guttation fluid from maize plants treated with TMX and grown in Alsace, France (data from Tables 37 & 39).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize plants grown from seeds treated with TMX	Guttation fluid, 90th centile (n = 41)	16152	129	8.6	Adult	8

Hazard quotients for concentrations of ΣTMX in guttation fluid from maize plants treated with TMX and grown in Alsace, France (data from Tables 37 & 39).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize plants grown from seeds treated with TMX	Pollen from plants	0	0.00	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of ΣTMX measured in guttation fluid was much greater than the NOAED for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from maize plants grown from treated seed was <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 26, 2016
SEJ	Yes	May 29, 2016

Narrative

Residues in bees were mostly <LOQ or small for TMX but clothianidin was detected in most specimens.

(Syngenta 2012b)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Lorraine (France) in 2010. Final Report Amendment 2. Syngenta Ltd, Bracknell, United Kingdom: Syngenta Ltd. (Unpublished Report). No. A9700B S10-01859. 340 p

The focus of this report was on the effects of dust from planting of maize seeds treated with TMX on honey-bees. This was a field study, which included the collection and analysis of guttation fluid from young maize plants and in pollen from maize plants and collected by forager bees, in soil, and in maize plants. The data for guttation fluids and pollen are the focus of this WoE.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in region of Lorraine, France from May 18, 2010 to 25 March 2011. There was one treatment and one control plot. The treated plot was 3.21 ha and the control was 1.92 ha (second seeding). Test and control plots were 2.78 km apart. Seeds of maize (var. NK Perform) were treated with TMX (0.68 mg/seed); fludioxonil 2.54 g/100 kg seed; and metalaxyl-M, 1.12 g/100 kg seed (measured concentrations). Seeds were sown on 18 May 2010. The treated field was sown at 109,845 seeds/ha (equivalent to 74.70 g TMX/ha). The control was sown with var. Gazelle (untreated) 124,542 seeds/ha (second drilling). A second drilling at the control field was necessary (4 June 2010) because maize seeds of the first drilling were destroyed by crows. Seeding was conducted with a Monosem pneumatic single seed drilling machine with deflector. Bees were present during seeding but deposition of dust was not measured (*weakness*). The use of appropriate crop protection chemicals (no neonicotinoids) was recorded and the same chemicals were applied to the test and control fields (Tables 44 to 47). Weather conditions were recorded (Tables 24–26). Guttation was observed more frequently in the morning and number of plants showing guttation was similar in treatment and control. Guttation fluid was collected from 1 June 2010 (emergence of maize plants) to 7 July 2010 (towards the end of guttation). If guttation was observed in the test field, droplets were collected from the leaf edges with capillary micropipettes (40 µL) and then transferred to Eppendorf tubes. Guttation fluid was sampled daily in the first week, twice in the second week and once in each following week after emergence of maize seedlings. If possible, on each sampling day, three samples of 0.5 mL were collected from a maximum of 200 plants not located within 1.5 m of the edge of the field. Samples were stored frozen (≤-18 °C) within 12 h after sampling until analysis. Guttation fluid was not sampled from the control plants *(potential weakness).* Pollen from plants and collected by bees was sampled on one day only (d-3 after flowering, 31 July 2010 and 10 August 2010 for the control). The tassel of a maize plant was held in a plastic bag and shaken for a few seconds to cause pollen-shed. At least five plants at each of 12 different locations in the test and control fields were sampled.	**2**

Responses 1-2: Quality of methods		Score
	Precautions were taken to avoid contamination. Pollen from each field was pooled, chilled during transport to the freezer, and subsequently stored deep frozen at ≤-18°C until analysis. Forager bees (ca. 50 from each of the six hives) were collected with a hand-vac. and directly frozen on dry ice. The subsamples were pooled, chilled during transport to the freezer and subsequently stored at ≤-18°C. Pollen loads from the forager bees were prepared at LAVES in Celle, Germany. Bees were thawed for a few minutes and the pollen loads were detached from the legs of the forager bees and placed into a vial. The pollen samples were unfrozen for <2 h during the preparation. Pollen was transferred back to the freezer immediately after preparation and stored at ≤-18°C. Conditions of storage of samples were recorded (Table 50). Samples for residue analysis were shipped frozen on dry ice to ADME, Vergènze, France for analysis. The analysis was well-described (Appendix 3). The standards for TMX and clothianidin were 99.7 and 98% pure. Isotopically labelled internal standards were not used. Analysis was by LC-MS/MS. The LOQs for TMX and clothianidin were 1 µg/kg (text) but Table 35 shows 5 µg/kg as the LOQ for pollen from bees. Recovery (no RSDs) of TMX and clothianidin from pollen was 92) and 83, respectively (Appendix 3, Table 1). For guttation fluid recovery (no RSDs) was 109% and 89, respectively. There was insufficient sample for analysis of pollen from bees foraging in the treated and control fields. Pollen from the control plants did not contain TMX or clothianidin. Pollen from the treated plants had concentration <LOQ. Residues of ΣTMX in guttation fluid declined over the period of sampling. Concentrations in guttation fluid remained high (above 13,000 µg/L from June 1 to June 6 but had declined to 18 µg/L on July 7 (Table 35).	
Use of GLP and QA/QC	The study was GLP with full QA and QC.	**4**
Transparency of data	Raw data were provided in the report.	**4**
Number of samples and replication	There was one site and one replicate	**1**
Duration of study sufficient to observe trends	For guttation fluid, the period of sampling was appropriate. Pollen was collected on one day only.	**3**
Overall evaluation of methods	Computed mean of above	**2.8**
Score for expert judgment on Quality of the study.	**1**	**2.80**

Relevance

Hazard quotients for concentrations of ΣTMX in guttation fluid from maize plants treated with TMX and grown in Lorraine, France (data from Tables 33 & 35).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize plants grown from seeds treated with TMX	Guttation fluid, 90th centile (n = 42)	34949	280	8.6	Adult	8

Hazard quotients for concentrations of ΣTMX in guttation fluid from maize plants treated with TMX and grown in Lorraine, France (data from Tables 33 & 35).

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Maize plants grown from seeds treated with TMX	Pollen from plants	0	0.00	8.6	Larva	8

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of ΣTMX measured in guttation fluid was much greater than the NOAED for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX measured in pollen from maize plants grown from treated seed was <NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 26, 2016
SEJ	Yes	May 29, 2016

Narrative

Residues in bees were mostly <LOQ or small for TMX but clothianidin was detected in most specimens.

(Syngenta 2013b)
Report: Syngenta. 2013. Thiamethoxam – A Field Study to Evaluate the Magnitude of Residues of Thiamethoxam and its Metabolite CGA322704 in Melon following a Granular Application of Actara® 5GR (A12180A) at Transplanting in Spain 2012 Final Report. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A12180A_10000 - A12180A (S12-02311). 119 p

The objective of this study was to determine the concentrations of TMX and its metabolite clothianidin in flowers, plants, nectar, and anthers of melon (*Cucumis melo*) under open field conditions in Spain after use as a granular formulation applied at transplant. Only the data in anthers and nectar are included in this WoE.

Responses 1-4: Quality of methods		**Score**
Experimental design and hypotheses	This study was well described and was carried out in region of Almansa, Spain in 2012. The history of pesticides used was provided (Table 2) and no neonicotinoids were used in the previous three y. The test treatments consisted of melon (*Cucumis melo* var. Sancho), treated once at transplanting (BBCH 12) with Actara® 5GR, a granular formulation containing 50 g TMX/kg (A12180A) at nominal rates of 1.2 g product/plant (39.6 g thiamethoxam/ha for 6600 plants per ha) or 2.0 g product/plant (66.0 g thiamethoxam/ha for 6600 plants per ha) and an untreated control (untreated with neonicotinoid insecticides). The analyzed content of TMX in the product was 0.559 % w/w. The application was conducted with plastic measures, with the test item applies as granules, un-dissolved in water, sprinkled around each plant at the surface of the soil at transplanting, and the variation was within 10% (Table 3). Transplanting was on 2012-06-16/17 and application was on 2012-06-18. All plots were located at the same field and were ca. 0.4 ha. The two test-item treated plots were separated by 30 m, and the distance from both treated plots to the control plot was 13 m. Plots were maintained during the field phase per normal agricultural practice. Ten mm of drip irrigation was applied daily. Weather data were reported (Table 6). From each plot, nectar, anther, flower and plant samples were taken twice, once at beginning of flowering (BBCH 62-63) on 2012-07-23, 35 d after treatment) and once at end of flowering (BBCH 67-69); plants, flowers and anthers on 2012-08-06, 49 d after treatment and nectar on 2012-08-08/10, 51-53 days after transplanting. At the first sampling of nectar, three independent pooled samples per test item treatment comprising ≥200 mg nectar each were collected from at least 12 different locations across the plot (control = one pooled sample). During the second sampling, one sample comprising 571 mg nectar was sampled in the test item treatment T1 instead of 3 x 200 mg, and in T2 one sample contained less than 200 mg. The nectar was collected either directly in the field or blossoms were collected from the plants, transported on blue ice to the laboratory for nectar extraction. Nectar was extracted from the flowers using 10-µL micropipettes. Anthers (with pollen) were collected from blossoms at each plot. On each sampling day, three independent pooled samples comprising ≥500 mg anthers per treatment were collected from at least 12 different locations across the plot (control = one pooled sample). Blossoms were collected from the plants, transported on blue ice to the laboratory for the removal of the anthers using forceps and scissors. Samples	**4**

Responses 1-4: Quality of methods			Score
	were frozen at -18C. Care was taken to avoid cross contamination. Storage and shipment conditions were recorded by use of data loggers (Table 15). Analysis was conducted at Eurofins Agroscience Services EcoChem GmbH in Niefern-Öschelbronn using standard methods and LC-MS/MS. Isotopically labeled internal standards were not used but standards were >98% pure. For anthers, the LOQ for TMX and clothianidin was 1 and 5 µg/kg, respectively, and recovery (RSD) of TMX and clothianidin from anthers was 102 (8%) and 96 (8%), respectively. For nectar, the LOQ for TMX and clothianidin was 0.5 and 1 µg/kg, respectively, and recovery (RSD) from nectar was 94 (3%) and 90 (7%), respectively (Data from Table 5, analytical report S12-02311). Neither TMX nor clothianidin were detected in the controls. Both TMX and clothianidin were detected in flower and plant samples. Clothianidin was detected at concentrations <LOQ in one nectar and two pollen samples (data from Table 11 and 12).		
Use of GLP and QA/QC	This was a GLP study with QA and QC.		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	There was a single site with one replicate for each of two treatments and one control.		**1**
Duration of study sufficient to observe trends	The duration of sampling was appropriate to the design of the study.		**4**
Overall evaluation of methods	Computed mean of above		**3.4**
Score for expert judgment on Quality of the study.		**1**	**3.40**

Relevance

Hazard quotients for concentrations of TMX in nectar and anthers from melon frown in Spain and treated at transplanting with TMX. (data from Tables 11 & 12)

Source of matrix	Sample	Conc. TXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Melon treated with 39.6 g TMX/ha	Nectar from plants max. (n = 4)	6.3	1.84	8.6	Adult	292
Melon treated with 39.6 g TMX/ha	Anthers from plants max. (n = 6)	2	0.25	8.6	Larva	124
Melon treated with 66 g TMX/ha	Nectar from plants max. (n = 6)	4.5	1.31	8.6	Adult	292
Melon treated with 66 g TMX/ha	Anthers from plants max. (n = 6)	3	0.37	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected from melon flowers exposed to 39.6 g TMX/ha at transplanting were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in anthers collected from melon flowers exposed to 39.6 g TMX/ha at transplanting were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in nectar collected from melon flowers exposed to 66 g TMX/ha at transplanting was that were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in anthers collected from melon flowers exposed to 66 g TMX/ha at transplanting were less than the NOAED for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2014)
Report: Syngenta. 2014. Thiamethoxam/Difenoconazole/Metalaxyl-M/Fludioxonil FS (A11642A) – Residue Levels in or on Canola (Flowers, Pollen and Nectar) from Trials Conducted in Canada During 2012 and 2013 Final Report. Guelph, Canada: Syngenta Ltd. (Unpublished Report). Report A11642A (TK0116694). 458 p

This was a field study where residues of TMX and the metabolite clothianidin were measured over two years of use on canola at four sites in Western Canada. Concentrations were measured in soil, flowers, pollen and nectar. Only the latter two were evaluated in this WoE.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The protocol for the study was well described. The study was conducted in western Canada between 2012 and 2013. There were four test sites where TMX was used as a seed-treatment for canola. These sites were in Dundurn, SK; Alvena, SK; Josephburg, AB; and Brandon, MB. Each field was divided into four plots. In 2012, the control plot was seeded with untreated canola seed and three plots were seeded with TMX treated canola seed. In 2013, the same control plot was planted with untreated canola seed and the treated plots were subdivided: one half of the plot was seeded with untreated canola and the other half was seeded with TMX treated canola. The history of pesticide applications at the sites showed no use of TMX in the previous 3 years but TMX was used at Dundurn in 2009 (p 17&18). The product used was HELIX XTra Seed Treatment, (A11642A) which contains TMX and the fungicides, difenoconazole, metalaxyl-M, (S-isomer) and fludioxonil. Seeds used in 2012 were canola var. 1841 RR and in 2013 canola var. 5525 CL (Table 16). Seeds were treated at a nominal rate of 438.3 g TMX/100 kg seed but individual batches of seed were analyzed. In 2012 the seed contained 433.2 g TMX/100 kg seed and in 2013, 393.7 g TMX/100 kg seed (Table 16). Cultivation and management of the sites were recorded (Table 2-9) and followed normal agricultural practice including pest management. Seeding was completed with an 8-row drill or a cone seeder. Soil characteristics and weather data were recorded (Sections 3.1.2.3-4 and 3.1.2.5). Samples were collected at or just after peak flowering (50-75% flowering to BBCH 68). Pollen was collected from at least 12 separate areas of the plot. Flowers were brushed over a sieve (unspecified mesh) to collect the pollen in a tray or Ziploc container. Once sufficient pollen was collected a paint-brush was used to transfer it into a vial that could then be weighed. The samples were then frozen (on-site freezer) as soon as feasible and transported to frozen storage (≤-10C) on the day of collection. Nectar was collected from at least 12 separate areas of the plot. To collect nectar, flowers were pushed open or petals removed to expose the nectar bulb so that micro-pipettes could be used to extract the nectar, which was then transferred to an Eppendorf tube until approximately 100 µL of sample was collected and then frozen as for pollen. Temperatures during transport in the field exceeded 0C but remained ≤ 10 °C after being frozen. The analysis of TMX and clothianidin was conducted at ALS Environmental in Edmonton, Alberta using a method based on Syngenta method REM 179.07 for LC-MS/MS and was well described. Isotopically labeled internal standards were not used but the standards	**3**

Responses 1-2: Quality of methods		Score
	used were >97% pure and the LOQ for both TMS and clothianidin was 1 µg/kg. Recovery (RSD) for TMX and clothianidin in nectar was 91 (12%) and 94 (16%) respectively in 2012 and 83 (11%) and 83 (17%) respectively in 2013. For pollen, it was 112 (NA) and 91 (NA) respectively in 2012 and 86 (6%) and 84 (17%) respectively in 2013 (data from Analytical Phase Report, Tables 3-6). In 2013, low recovery of TMX (49%) was reported in pollen in one set of analyses (Table 7) (*potential weakness*). Residues of TMX and clothianidin were detected in flower and soil samples in 2012 and only TMX was detected in soil in 2013.	
Use of GLP and QA/QC	The study was conducted under GLP with QA and QC. Exceptions such as history of pesticide use and weather were listed.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There were four sites studied over two years. Three pseudoreplicated samples were taken at each site in 2012 and 2013 were but not all sites were sampled.	**2**
Duration of study sufficient to observe trends	Sampling appeared to cover less than 50% of the flowering period.	**1**
Overall evaluation of methods	Computed mean of above	**2.8**
Score for expert judgment on Quality of the study.	**1**	**2.80**

Relevance

Hazard quotients for concentrations of ΣTMX in nectar and pollen from canola grown in Western Canada from seeds treated with TMX. (data from Tables 11-14 in the Analytical Phase Report)

Source of matrix	Sample	Conc. ΣTXM in µg/kg or L	Dose ng/bee	Chronic NOAED ng/bee/d	Life-stage	mg diet/d
Canola treated with 433.2 g TMX/100 kg in 2012	Nectar from plants max. (n = 9)	2.5	0.73	8.6	Adult	292
Canola treated with 433.2 g TMX/100 kg in 2012	Pollen from plants max. (n = 9)	9.0	1.12	8.6	Larva	124
Canola treated with 383.7 g TMX/100 kg in 2013	Nectar from plants max. (n = 23)	0	0.00	8.6	Adult	292
Canola treated with 383.7 g TMX/100 kg in 2013	Pollen from plants max. (n = 23)	0	0.00	8.6	Larva	124

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure. Where clothianidin was measured in the matrix, the amount of clothianidin was normalized to TMX (divide by 0.86) and the sum presented as ΣTMX.

Response 1: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of ΣTMX measured in nectar from canola grown from seed treated with TMX in 2012 and 2013 resulted in exposures that were less than the NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**

Score for expert judgment on relevance of the results.	**1**	**0.00**

Response 2: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of ΣTMX measured in pollen from canola grown from seed treated with TMX 2012 and 2013 resulted in exposures that were less than the NOAED for honeybees.	**0**
Overall evaluation relevance	Computed mean of above score(s)	**0.00**
Score for expert judgment on relevance of the results.	**1**	**0.00**

Expert judgment		
QA	Yes	May 25, 2016
SEJ	Yes	May 29, 2016

Risks to honeybees resulting from exposure to dusts containing TMX

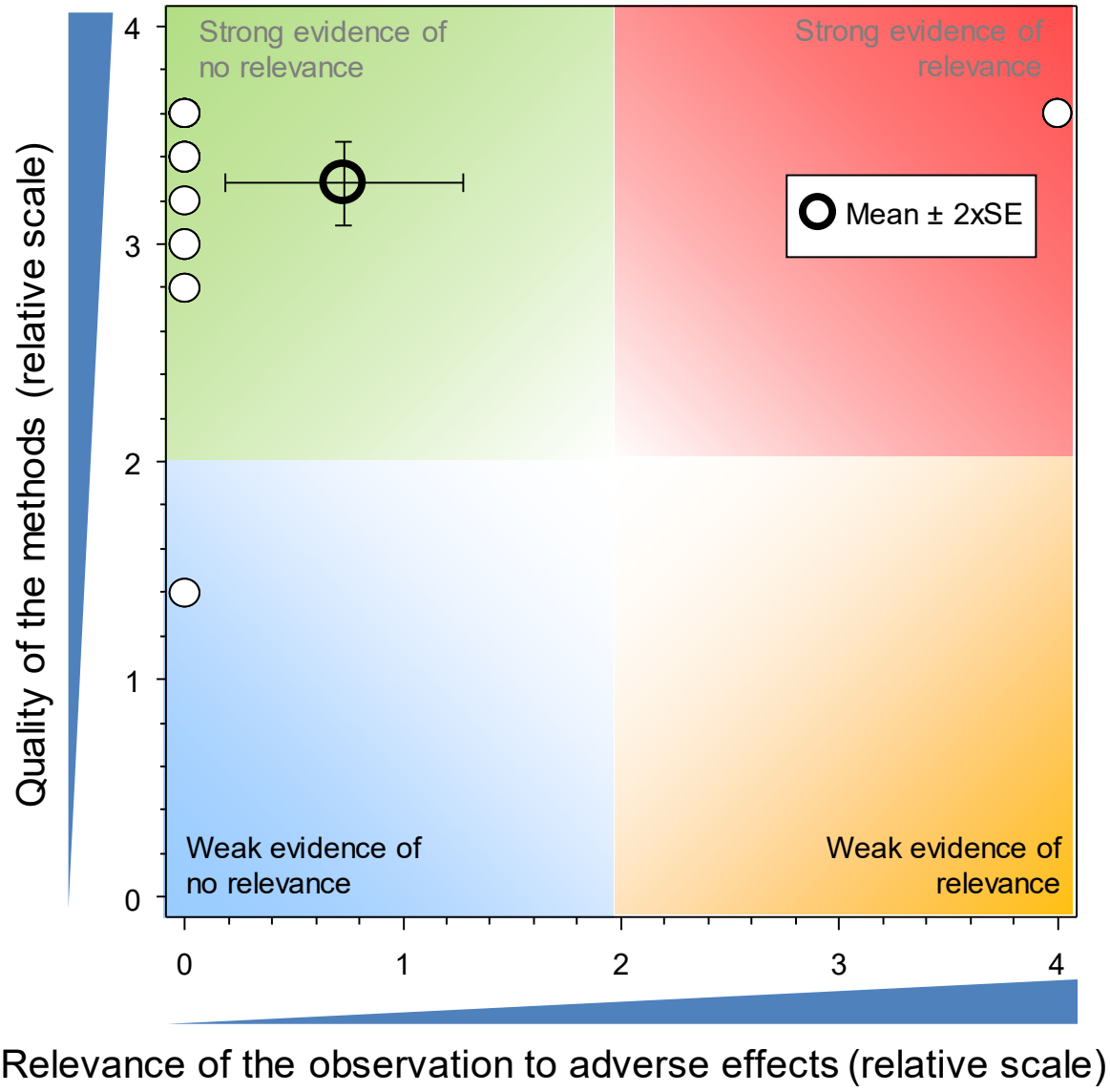
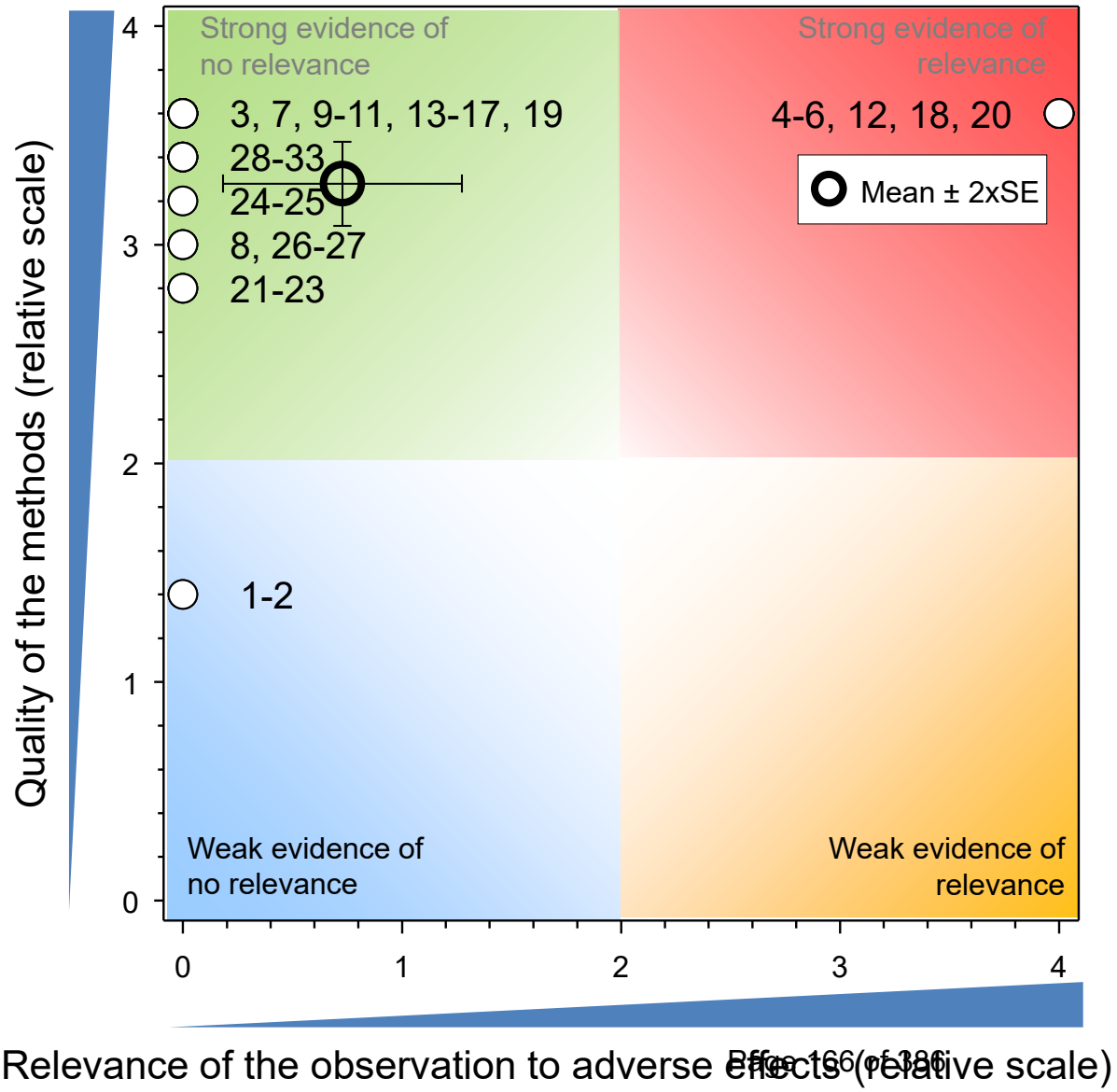


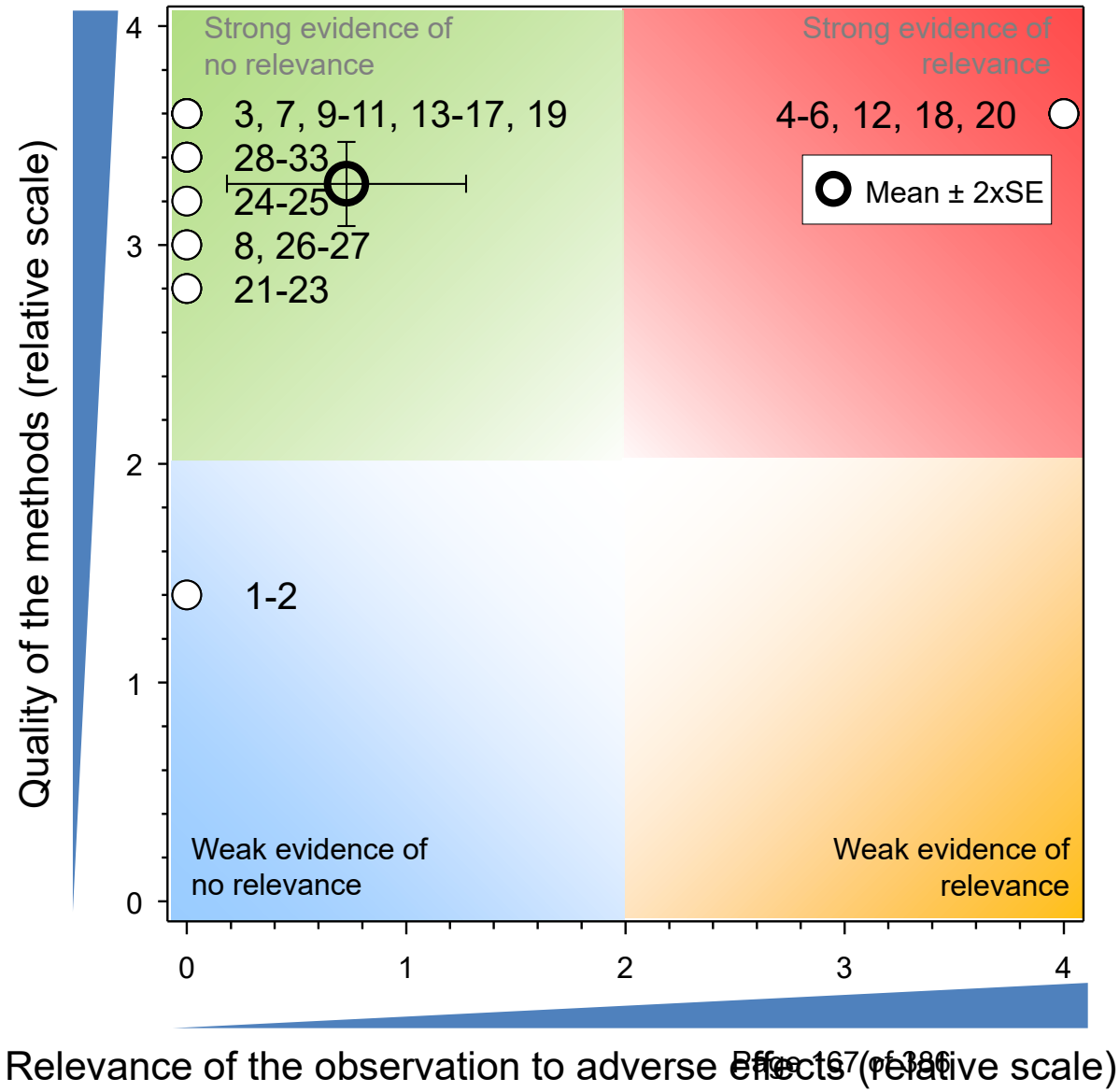
Figure 3. Quality and relevance of exposure values from controlled field studies on deposition of dust during drilling of seeds treated with TMX, n = 33. Symbols may obscure others, see this SI below for all responses. There were no points in the obscured by the legend in the upper right quadrant.

Risks to honeybees resulting from exposure to dusts containing TMX



1 = (Biocca et al. 2015) Resp 1
2 = (Biocca et al. 2015) Resp 2
3 = (Syngenta 2007e) Resp 1
4 = (Syngenta 2007e) Resp 2
5 = (Syngenta 2008b) Resp 1
6 = (Syngenta 2008b) Resp 2
7 = (Syngenta 2008b) Resp 3
8 = (Syngenta 2008a) Resp 1
9 = (Syngenta 2010g) Resp 1
10 = (Syngenta 2010g) Resp 2
11 = (Syngenta 2010g) Resp 3
12 = (Syngenta 2010g) Resp 4
13 = (Syngenta 2010f) Resp 1
14 = (Syngenta 2010f) Resp 2
15 = (Syngenta 2010f) Resp 3
16 = (Syngenta 2010f) Resp 4
17 = (Syngenta 2010f) Resp 5
18 = (Syngenta 2010f) Resp 6
19 = (Syngenta 2010e) Resp 1
20 = (Syngenta 2010e) Resp 2

Risks to honeybees resulting from exposure to dusts containing TMX

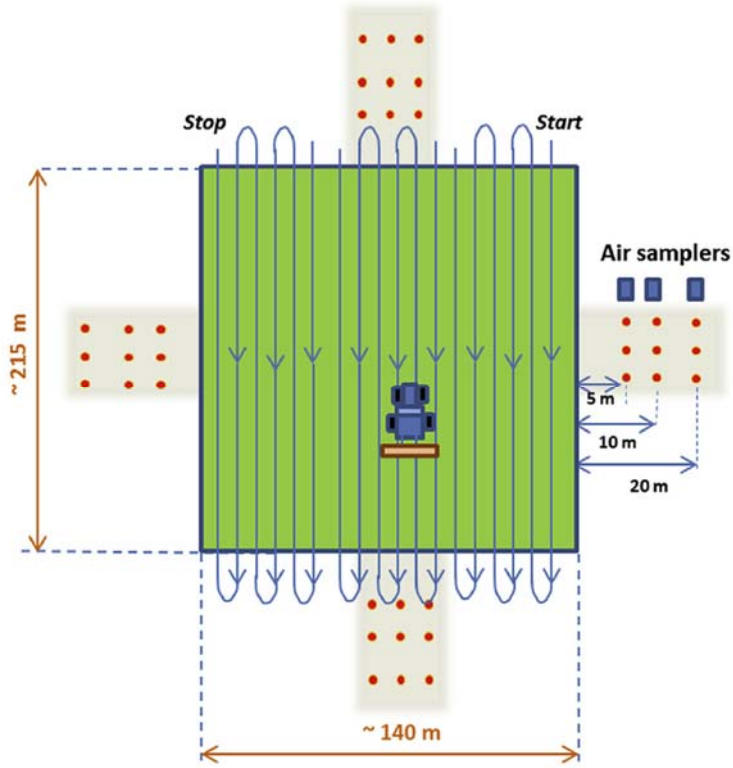


21 = (Syngenta 2010i) Resp 4
22 = (Syngenta 2010i) Resp 5
23 = (Syngenta 2010i) Resp 6
24 = (Syngenta 2011c) Resp 1
25 = (Syngenta 2011c) Resp 2
26 = (Syngenta 2011a) Resp 1
27 = (Syngenta 2011a) Resp 2
28 = (Syngenta 2012c) Resp 1
29 = (Syngenta 2012c) Resp 2
30 = (Syngenta 2012e) Resp 1
31 = (Syngenta 2012e) Resp 2
32 = (Syngenta 2012e) Resp 3
33 = (Syngenta 2012e) Resp 4

(Biocca et al. 2015)
Paper: Biocca M, Fanigliulo R, Gallo P, Pulcini P, Pochi D. 2015. The assessment of dust drift from pneumatic drills using static tests and in-field validation. Crop Protection 71:109-115.

The objectives of the study were to quantify the ground deposition rate of clothianidin, fipronil, imidacloprid and thiamethoxam from maize seeds treated with these neonicotinoids. The study was conducted with a stationary drill in a "wind tunnel" and drilling in a field. The stationary drilling was deemed to be lower tier and only the data from the field work are assessed here. Samples in air were not included in the WoE. Only TMX was considered for this WoE.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The test was, in general, poorly described. The test was conducted on the experimental farm of CRA-ING in 2010. The field component for TMX was conducted between April 21 and June 8, 2010. The test fields were 3 ha rectangular plots (~140 x 215 m) but the previous use of the fields was not reported (*potential weakness*). The drill was a six-row precision pneumatic drill, "Gaspardo Magica", used with and without a device for the reduction of the drift of dust. Seeding was assumed to follow good agricultural practices and seed density of 75,000 seeds/ha was used. Climatic conditions during seeding were reported (Table 1) and the wind speed was 1.0-2.2 m/sec for the TMX drift studies. Commercial maize seed (Pioneer Hy-Bred PR32G44) was dressed with four insecticides (not clear but assumed to be done separately, even though the data were reported as combined values). The dressings were (Gaucho™, a.s.: imidacloprid; Poncho™, a.s. = clothianidin; **Cruiser™, a.s.: TMX**, Regent™, a.s.: fipronil) and a fungicide (Celest™, a.i.: fludioxonil and metalaxyl); only TMX is included in the WoE. According to the manufacturers, the application doses of a.s. were 1.00 mg/seed for imidacloprid, 1.25 mg/seed for clothianidin; **0.60 mg/seed for TMX** and 0.50 mg/seed for fipronil. Abrasion loss from the seed was assessed by means of the standard Heubach test and the results were less than the reference limit of 3 g/100 kg. The drilling was replicated once per a.s. with and without the deflector. The layout of the plots was shown in Fig. 2 (see diagram below). **Primary drift** (deposition) of TMX was sampled in Petri-dishes (unstated size) containing an unstated volume of a mixture of acetonitrile and water (1:1, v/v). Nine samplers each were placed onto each of the four sides of the field. Each sampling block consisted of 9 dishes placed in three rows at distances of 5, 10, and 20 m from the edge of the field for a total of 36 dishes (see diagram). Air samplers were deployed but were not analyzed in the WoE; however, the authors used these data to develop models for estimation of deposition. When the dishes were collected and how the samples were transported and stored were not reported (*potential weakness*). Because the samples were held in the mixture of acetonitrile and water (1:1), degradation would be minimal. Samples were not reported to be inspected for the presence of large particles that would be biologically unavailable to bees (*weakness*).	**1**

	All samples were analyzed at CRA-PAV. Active substances were extracted from the samples with acetonitrile and analyzed with an LC-MSD. The conditions of analysis were well described. It was stated that the "methods were validated in compliance with GLP (Good Laboratory Practice)" but no information on the reference or internal standards was provided (*weakness*). The LOQ and recovery were not reported (*weakness*). Controls and field blanks were not reported (*weakness*).  The concentrations measured in the samples from the seeder without the deflector were, in all cases, more than with the deflector. Amount of deposition decreased with distance from the edge of the field. Depositions were normalized to µg a.s./m^2 but the formula for this and the area of the Petri dishes was not provided (*weakness*). For this WoE, these were converted to g/ha (divide by 100 [from g/ha = µg/m^2*10,000/1,000,000]) for comparison to toxicity values.	
Use of GLP and QA/QC	The analytical component of the study was apparently conducted under GLP. The other components of the study were not GLP and were poorly described.	**1**
Transparency of data	Raw data were not provided and only summary data (± SE) were shown in a graph (Fig. 3, lower). Data for the individual chemicals were not reported and SI was not provided. It is thus not possible to evaluate the individual chemicals and it is not clear if they were summed or averaged (*weakness*). For the purposes of the WoE, it was assumed that all of the residue collected was TMX.	**0**
Number of samples and replication	There was one site with one replicate and four groups of samples at three distances from the field.	**1**

Duration of study sufficient to observe trends	Duration of the study is appropriate to the design and objectives.		**4**
Overall evaluation of methods	Computed mean of above		**1.4**
Score for expert judgment on Quality of the study.		**1**	**1.40**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (Fig. 3 lower)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Seeder without deflector	Mean value at 5 m distance (n=12)	0.090	0.02	5
Seeder with deflector	Mean value at 5 m distance (n=12)	0.035	0.01	5

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The mean rate of TMX deposited 5 m from mechanical seeder without a deflector sowing corn treated with TMX was <the NOAER.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The mean rate of TMX deposited 5 m from mechanical seeder with a deflector sowing corn treated with TMX was<the NOAER.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 30, 2016

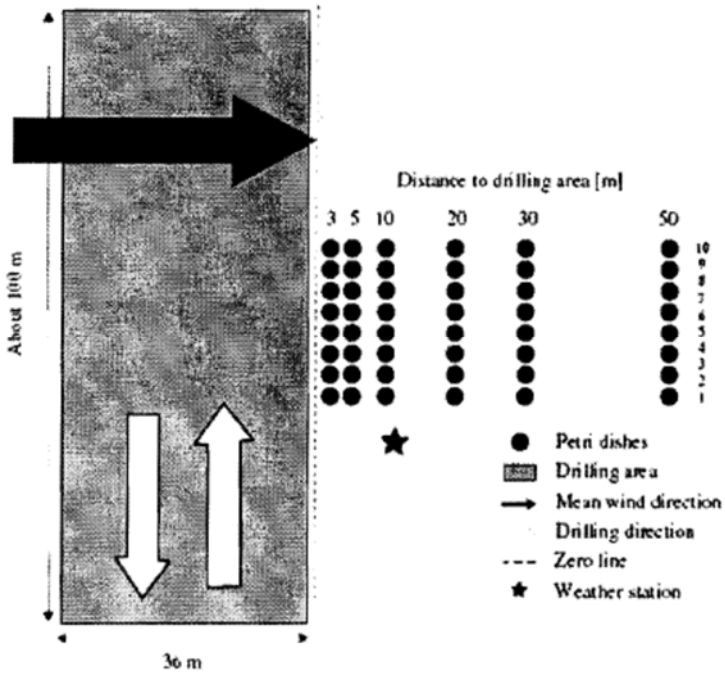
Narrative:

The experimental section of this paper was virtually word-for-word the same as that in Pochi et al. 2012[21] except that the methods and results for the deposition data were included and the modeling (not assessed) was different. Biocca was an author on both papers and the 2015 paper was self-plagiarized. The paper by Pochi et al. (2012) was not used in the WoE because there were no depositional data.

[21] Pochi D, Biocca M, Fanigliulo R, Pulcini P, Conte E. 2012. Potential exposure of bees, *Apis mellifera* L., to particulate matter and pesticides derived from seed dressing during maize sowing. *Bulletin of Environmental Contamination and Toxicology* 89:354-361.

(Syngenta 2007e)
Report: Syngenta. 2007. Thiamethoxam: Deposition of Dust from Pneumatic Drilling of A10590C Treated Maize Seed in France During 2006. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_3445. 48 p

This study was conducted to evaluate drift of dust resulting from the seeding of maize treated with TMX with a pneumatic driller. Deposition samples were collected downwind of the driller and at the outlet of the exhaust fan. Only the deposition samples were assessed in this WoE.

Responses 1-2: Quality of methods		**Score**
Experimental design and hypotheses	The study was carried out at Fougere and the Tierce field station, France. The plot was 0.36 ha and there were four drillings on the same site but at separate times. The site had been used the previous year to grow maize. Seeding was done on the 19th and 21st of April 2006. The treated maize seed was var. Gazelle and the formulation used contained 420 g TMX/L. Seeds were analyzed and the treatment rate was 185 g TMX/100 kg seed. The driller was a Nodet Gougis Pneunasen II pneumatic seed driller and the seeds were drilled at 85,000/ha. Wind speeds varied between 0.4 and 4 m/sec during drilling. Weather conditions were recorded during drilling (Appendix 1, Tables 18-21). Application rate was 54 g TMX/ha. Six rows of 10 Petri-dishes (143.14 cm^2) were set up in the centre, downwind of the test plot at distances of 3, 5, 10, 20, 30, and 50 m from the zero line of the first pass (see diagram below). Each dish contained 50 ml of a 1:1 solution of glycerol and ultrapure water. Samples were covered with lids and collected after drilling.  After deposition, samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. Samples were frozen	**4**

	within 12 h of collection (-18C) and shipped frozen to Syngenta Jealott's Hill, UK for analysis. Field recovery samples were treated in the same way. Analytical method was reported separately [22]. The glycerol-water solution was analyzed directly with a high-performance column switching liquid chromatography with triple quadrupole mass spectrometry detection (LC-LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard was 99.5% pure. The LOQ was 1 ng per dish (= 0.01 ng/mL). Recovery ranged from 85-103% with an RSD of ≤2–21%. The recovery for the field-spike samples ranged from 91 to 104%. Raw residue data were converted from percent of application rate (54 g/ha) to g/ha for comparison to the NOAER. The greatest mean deposition at any distance from the zero line of the first pass was used to calculate the trial mean.	
Use of GLP and QA/QC	This was a GLP study with clear protocol, and QA and QC.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	The study was conducted at one site with two replicates each with and without a dust-deflector.	**2**
Duration of study sufficient to observe trends	Duration was appropriate for the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.6**
Score for expert judgment on Quality of the study.	**1**	**3.60**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (Tables 2,4, 6 & 8)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Seeder without deflector	Mean value at 5 & 5 m distance from the zero line (n = 20)	0.44	4.37	0.1
Seeder with deflector	Mean value at 10 & 10 m distance from the zero line (n = 20)	0.019	0.19	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

[22] Syngenta. 2006. Thiamethoxam; Validation of a Method and Sample Analyis of the Depositon of Dust from Pneumatic Drilling of Treated Maize Seed. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_2994. 66 p

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited 5 m from the zero line of the first pass seeded with a seeder with no deflector resulted in exposures that were >NOAER for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

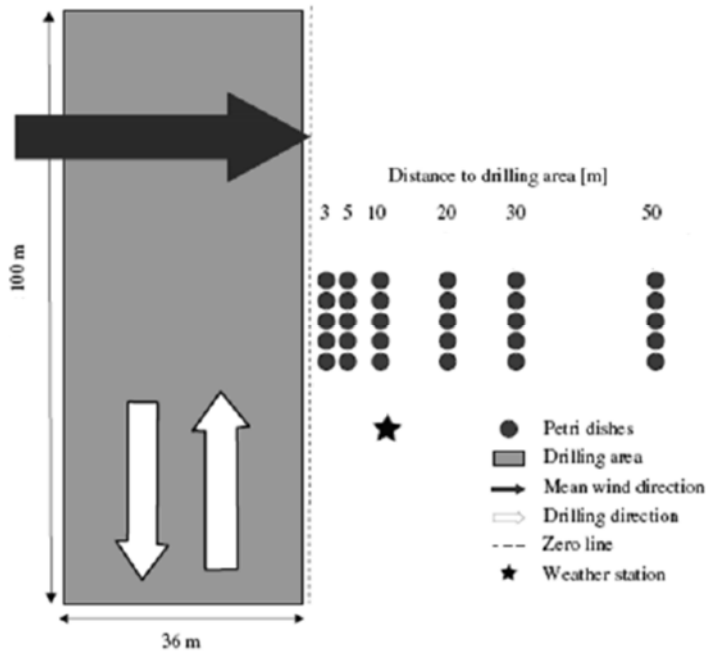
Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited 10 m from the zero line of the first pass seeded with a seeder with a deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 26, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2008b)
Report: Syngenta. 2008. Thiamethoxam: Deposition of Dust from Pneumatic Drilling of A9700B+A9638A Treated Maize Seed in France During 2008. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B. 57 p

This study was conducted to evaluate drift of dust resulting from the seeding of maize treated with TMX with a pneumatic driller. Deposition samples were collected downwind of the driller and at the outlet of the exhaust fan. Only the deposition samples were assessed in this WoE.

Responses 1-3: Quality of methods		**Score**
Experimental design and hypotheses	The study was carried out at Cheffes, France. The plot was 0.36 ha and there were three drillings on the same site but at different times. Seeding was done on the 10th of June 2008. The treated maize seed was var. Altius and the formulation used contained 350 g TMX/L (A9700B+A9638A) and a presumed fungicide. Seeds were analyzed and the mean (n = 4) treatment rate was 280 g TMX/100 kg seed. The driller was a Nodet Gougis Pneunasen II pneumatic seed driller and the seeds were drilled at 108,000/ha. In one trial no deflector was used, in the second a dual tube deflector was used and in the third, a dust cyclone was used. Each trial was replicated twice. Wind speeds varied between 0.4 and 4.9 m/sec during drilling. Weather conditions were recorded during drilling (Appendix 1, Table 21-26). Application rate was 71 g TMX/ha. Six rows of five Petri-dishes (143.14 cm^2) were set up in the centre, downwind of the test plot at distances of 3, 5, 10, 20, 30, and 50 m from the zero line of the first pass (see diagram below). Each dish contained 50 ml of a 1:1 solution of glycerol and ultrapure water. Samples were covered with lids and collected after drilling. After deposition, samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. Samples were frozen (-20C) within 1 h of collection and shipped frozen to Eurofins/ADME Bioanalyses, France for analysis. Field recovery samples were treated in the same way. Analytical method was reported separately[2]. The glycerol-water solution was analyzed directly with a high performance column switching liquid chromatography with triple quadrupole mass spectrometry detection (LC-LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard was 99.5% pure. The LOQ was 1 ng per dish (= 0.01 ng/mL). Recovery ranged from 93–100% with RSDs of 10 and 7%. The recovery for the field-spike samples ranged from 87 to 96%. Raw residue data were converted from percent of application rate (71 g/ha) to g/ha for comparison to the NOAER. The greatest mean deposition at any distance from the zero line of the first pass was used to calculate the trial mean.	**4**

		
Use of GLP and QA/QC	This was a GLP study with clear protocol, and QA and QC.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	The study was conducted at one site with two (time independent) replicates each with one of two deflectors and without a dust-deflector.	**2**
Duration of study sufficient to observe trends	Duration was appropriate for the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.6**
Score for expert judgment on Quality of the study.	**1**	**3.60**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (Tables 2, 4, 6, 8, 10 & 12)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Seeder without deflector	Mean value at 3 & 5 m distance from the zero line (n = 10)	0.76	7.56	0.1
Seeder with dual tube deflector	Mean value at 3 & 10 m distance from the zero line (n = 10)	0.22	2.24	0.1
Seeder with cyclone deflector	Mean value at 3 & 3 m distance from the zero line (n = 10)	0.10	0.96	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 and 5 m from the zero line of the first pass seeded with a seeder with no deflector resulted in exposures that were >NOAER for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 and 10 m from the zero line of the first pass seeded with a seeder with a dual tube deflector resulted in exposures that were >NOAER for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited 3 m from the zero line of the first pass seeded with a seeder with a cyclone deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

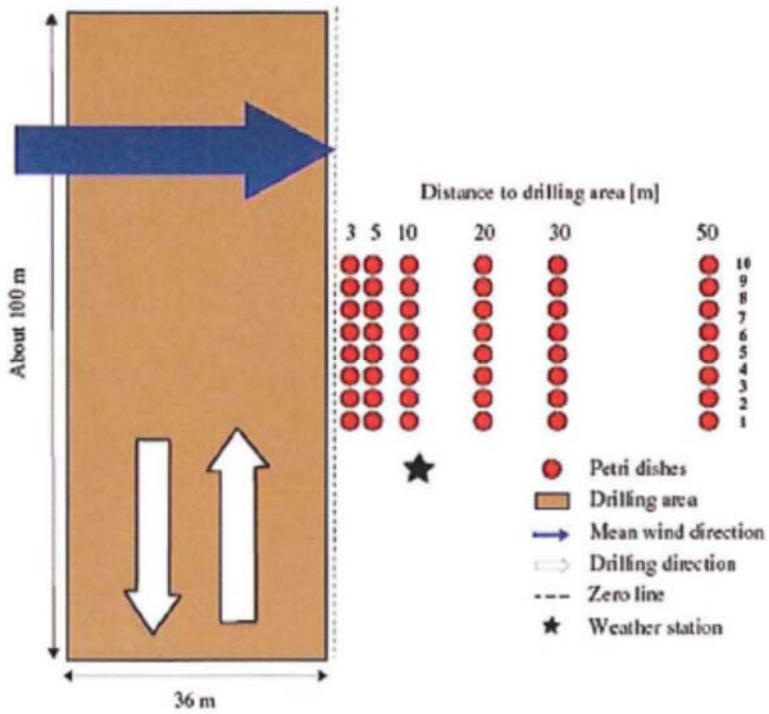
Expert judgment		
QA	Yes	May 26, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2008a)
Report: Syngenta. 2008. Thiamethoxam; Deposition of Dust from Pneumatic Drilling of A9700B Treated Maize Seed in France During 2005. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10842. 27 p

This study was conducted to evaluate drift of dust resulting from the seeding of maize treated with TMX with a pneumatic driller. Deposition samples were collected downwind of the driller and at the outlet of the exhaust fan. Only the deposition samples were assessed in this WoE. The analytical component of the study was provided in a separate report[23].

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	The study was carried out at Fougere, France. The plot was 0.36 ha and there were four drillings on the same site but at different times. In one of the drillings, the driller was equipped with a filter for trapping emitted seed dust in an air filter. Those results are not discussed in this WoE. The site had been used the previous year to grow maize. Seeding was done on the 26/27th of October 2005. The treated maize seed was var. Gazelle and the formulation used contained 339 g TMX/L (A9700B analyzed). Seeds were not analyzed (*weakness*). The driller was a Nodet Gougis Pneunasen II pneumatic seed driller and the seeds were drilled at 93,333 seeds/ha. No deflector was used. The trial was replicated three times. Wind speeds varied between 0 and 5.4 m/sec during drilling. Weather conditions were recorded during drilling (Section 5.2). Application rate was 84 g TMX/ha. Six rows of five Petri-dishes (143.14 cm^2) were set up in the centre, downwind of the test plot at distances of 3, 5, 10, 20, 30, and 50 m from the zero line of the first pass (see diagram below). Each dish contained 50 ml of a 1:1 solution of glycerol and ultrapure water. Samples were covered with lids and collected after drilling. After deposition, samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. Samples were frozen (-20C) within 12 h of collection and shipped frozen to Syngenta, Jealott's Hill, UK for analysis. Field recovery samples were treated in the same way. Analytical method was reported separately[3]. The glycerol-water solution was analyzed directly with a high performance column switching liquid chromatography with triple quadrupole mass spectrometry detection (LC-LC-MS/MS). Isotopically labelled internal standards were not used but the reference standard was 99.5% pure. The LOQ was 1 ng per dish (= 0.01 ng/mL). Recovery ranged from 75–81% with RSDs of 13–7%. The recovery for the field-spike samples ranged from 84 to 96%. Raw residue data were converted from percent of application rate (84 g/ha) to g/ha for comparison to the NOAER. The greatest mean	**3**

[23] Syngenta. 2006. Thiamethoxam: Validation of a Method and Sample Analysis of Deposition of Dust from Pneumatic Drilling of Treated Maize Seed. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_2995 13 p

	deposition at any distance from the zero line of the first pass was used to calculate the trial mean.  	
Use of GLP and QA/QC	This was a GLP study with clear protocol but no QA and limited QC.	**2**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	The study was conducted at one site with three time-independent replicates each with no deflector and one with a filter.	**2**
Duration of study sufficient to observe trends	Duration was appropriate for the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3**
Score for expert judgment on Quality of the study.	**1**	**3.00**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (Tables 3, 5, & 7) in Report CGA293343_2995

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Seeder without deflector	Mean value at 5, 3, & 5 m distance from the zero line (n = 30)	0.49	0.49	1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

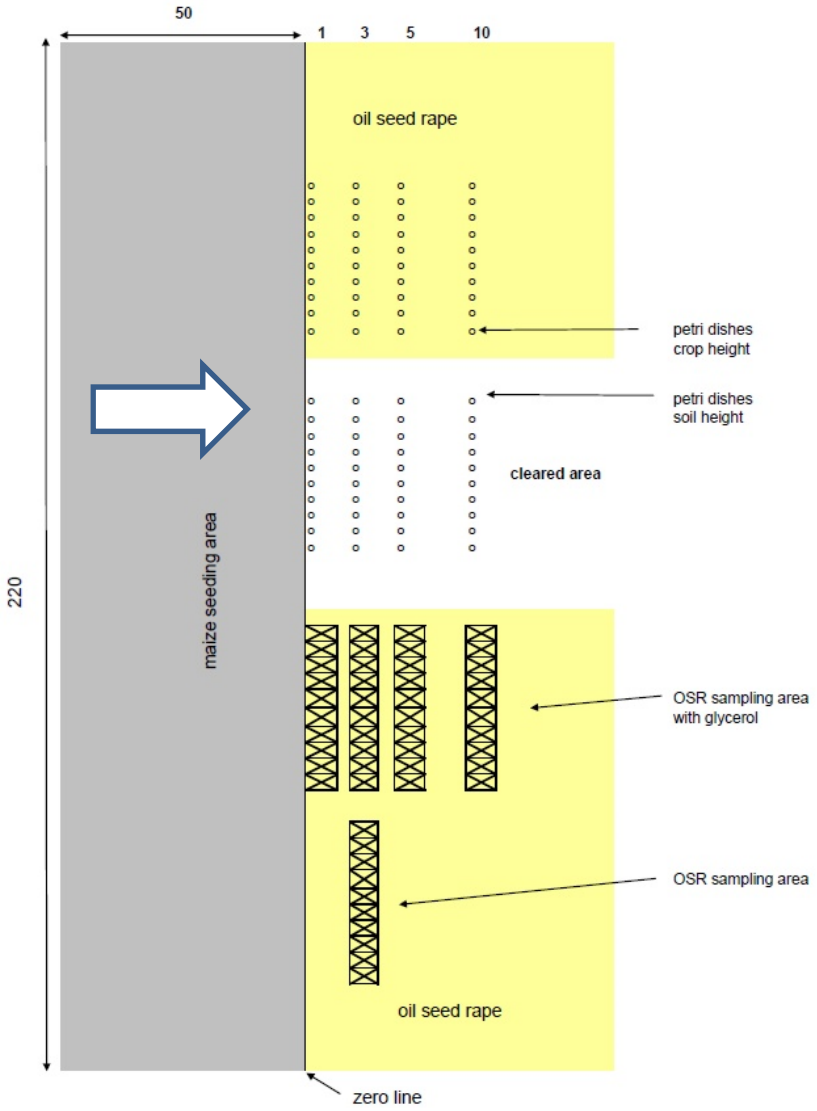
Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 and 5 m from the zero line of the first pass seeded with a seeder with no deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 26, 2016
SEJ	Yes	May 29, 2016

(Syngenta 2010g)
Report: Syngenta. 2010. Evaluation of deposition of seed treatment particles abraded from "PRODUCT" dressed maize seeds emitted during sowing, in adjacent oilseed rape and bare soil areas Final Report Amendment No. 1. Frankfurt am Main, Germany: Syngenta Ltd. (Unpublished Report). Report A9700B_10906. 69 p

This study was conducted to evaluate drift of dust resulting from the seeding of maize treated with TMX with a pneumatic driller. Deposition samples were collected downwind of the driller over bare soil and on a flowering crop of oilseed rape (OSR).

Responses 1-4: Quality of methods		**Score**
Experimental design and hypotheses	The study was carried out at two locations in the Lower Saxony, Germany. The seeded plots were 0.98 and 1.01 ha. OSR was seeded on 2009-05-04. Maize seeding was done on 2009-07-04 and 2009-07-05 during OSR flowering (BBCH 67). The var. of the treated maize seed was not reported. Section 3.1 (p. 13) reported 0.61 mg of "compound" = TMX per seed or 154.82 g TMX/100 kg seeds. The driller was an Amazone 602-K and seeds were drilled at 96,700 and 97,600 seeds/ha. A JKI deflector (JKI V-number 255-34) with a 90% dust reduction was fitted to the seeder. Mean wind speeds varied between 2.2 and 4.1 m/s and 1.3 and 4.7 m/sec, for sites 1 and 2, resp. during drilling. Weather and wind conditions were recorded during drilling (Appendix 1, Tables 5 and 6, Figures 15 and 16). Application rate was 58.99 and 59.54 g TMX/ha on sites 1, and 2, resp. Four rows of ten Petri-dishes (143.14 cm^2) were set up downwind of the test plot at distances of 1, 3, 5, and 10 m from the zero line (the seeded row closest to the OSR crop) (see diagram below). The average distance between the nominal 1 m row and zero line was 2.43 and 1.82 m for field sites 1 and 2, as it was not possible to drill closer to the OSR. Each dish contained 75 ml of a 1:1 solution of glycerol and ultrapure water. Samples were covered with lids and collected after drilling. One set of collectors was placed on the soil and another set of collectors was placed on posts at the height of the OSR crop. The height of the Petri dishes above soil was 145 cm and 135 cm, on field 1 and 2, resp. In addition to the Petri-dishes, samples of OSR crop at BBCH-67 (whole plants) were collected for analysis. All of the plants in a predefined 50x50 cm area were sample for analysis. Ten replicate samples were taken at 3 m from the drilled field. At another location, the plants were hand-sprayed with a 1:1 solution of glycerol and ultrapure water prior to maize seeding. This was done to reduce the loss of dust from the plants. Here ten replicate samples were taken at 1, 3, 5, and 10 m from the drilled field. After deposition, Petri-dish samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. Plants were carefully removed and placed into a polyethylene container (34 L), taking care to avoid disturbance and minimizing the possibility for dislodging dust. All samples were frozen (-18C) within 3 h of collection. Frozen samples were shipped to eurofins-ADME Bioanalyses for analysis. Field recovery samples held open upwind of the drilling were treated in the same way.	**4**

	Analytical method was reported separately[3]. The glycerol-water solution was analyzed directly with a high-performance column switching liquid chromatography with triple quadrupole mass spectrometry detection (LC-LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard was 99.5% pure. The LOQ for the dish collectors was 0.001 µg/dish and, for the plant samples, was 0.001 mg/kg. Mean recovery for the Petri-dish samples was 91% with a RSD of 10.4% and for the plant samples was 92% with an RSD of 11.4% (Appendix 2, Table 7).  Raw residue data were converted from percent of application rate (59 g/ha) to g/ha for comparison to the NOAER. The greatest mean deposition at any distance from the zero line was used to calculate the trial mean.	
Use of GLP and QA/QC	This was a GLP study with QA and QC.	**4**
Transparency of data	All raw data were provided.	**4**

Number of samples and replication	The study was conducted at two sites with one replicate.		**2**
Duration of study sufficient to observe trends	Duration was appropriate for the objectives of the study.		**4**
Overall evaluation of methods	Computed mean of above		**3.6**
Score for expert judgment on Quality of the study.		**1**	**3.60**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (p 24-25).

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Seeder with deflector, collector at soil level.	Max mean value at 1 & 5 m distance from the zero line (n = 20)	0.03	0.31	0.1
Seeder with deflector, collector at height of crop.	Max mean value at 1& 10 m distance from the zero line (n = 20)	0.03	0.30	0.1
Seeder with deflector, residues on plant (no glycerol-water).	Max mean value at3 m distance from the zero line (n = 20)	0.06	0.60	0.1
Seeder with deflector, residues on plant (glycerol-water).	Max mean value at 1 & 1 m distance from the zero line (n = 20)	0.11	1.14	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 1 and 5 m from the zero line of the field seeded with a seeder with a deflector resulted in exposures that were<NOAER for honeybees at soil level.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 1 & 10 m from the zero line of the field seeded with a seeder with a deflector resulted in exposures that were <NOAER for honeybees at the height of the crop.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited 3 m from the zero line of the field seeded with a seeder with a deflector resulted in exposures that were <NOAER for honeybees on the OSR crop (no glycerol/water used).	**0**

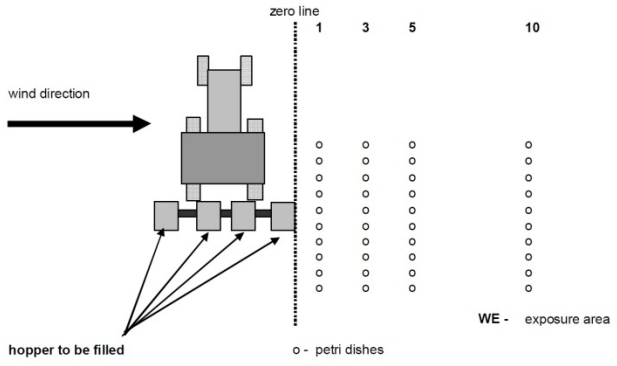
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

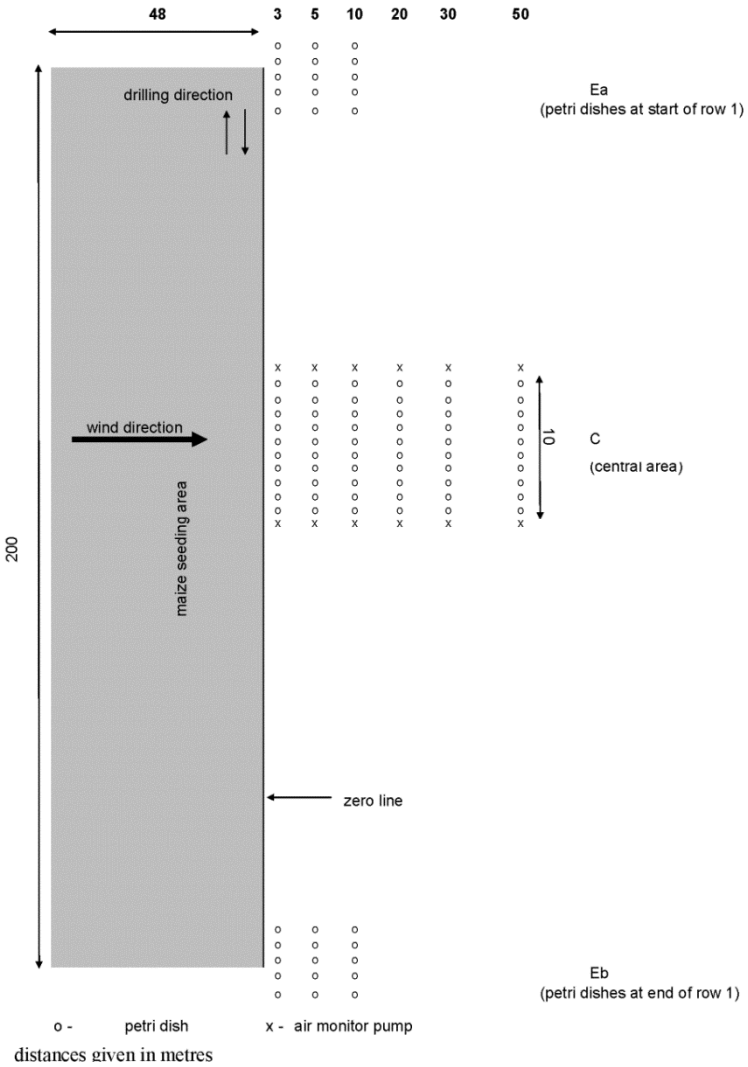
Response 4: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited 1 & 1 m from the zero line of the field seeded with a seeder with a deflector resulted in exposures that were >NOAER for honeybees on the OSR crop (glycerol/water used as a sticker on the crop).		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

Expert judgment		
QA	Yes	May 27, 2016
SEJ	Yes	May 2016

(Syngenta 2010f)
Report: Syngenta. 2010. Thiamethoxam - Investigating the Deposition of Dust from Pneumatic Drilling of A9700B Treated Maize Seeds in France during 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10917. 131 p

This study was conducted to evaluate drift of dust resulting from the seeding of maize treated with TMX with a pneumatic driller. Deposition samples were collected downwind of the driller. Samples of dust deposited because of filling the hoppers were analyzed as well. Personal air-samplers were used to collect samples of dust from air but were not included in this WoE and toxicity data for concentrations in air were not available. Analyses of residues in an air filter attached to the seeder were not included in the WoE.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The study was carried out in Angers (Loire valley), France. The seeded plots were 0.96 ha and there were four fields. Seeding was done between 2009-10-13 and 2009-10-14. The var. of the treated maize seed was NK Factor. Seeds were treated with Cruiser 350 FS. Concentration on the seeds was measured at 0.65 mg TMX/seed. Dust generated during seed hopper filling was monitored by deposition in closely situated downwind Petri-dishes. The driller was a Monosem NG plus 4 seed driller and seeds were drilled at 110,081 seeds/ha. For fields 1 & 3, a Syngenta deflector was fitted to the seeder. In fields 2 & 4, a Monosem deflector was used. Mean wind speeds varied between 0.99 and 5.1 m/sec during drilling (p. 14, and Tables 7-10). Weather and wind conditions were recorded during drilling (Tables 4 & 5 and Figures 24-27). Application rate was 71.6 g TMX/ha on all plots. Six rows of ten Petri-dishes (143.14 cm^2) were set up downwind of the test plot at distances of 3, 5, 10, 20, 30, and 50 m from the zero line (see diagram below). In addition, three rows of five Petri-dish samplers at 3, 5 and 10 from the zero line were set up at both ends of each seeded plot. To assess for post-application remobilization, one row of 10 Petri-dishes were set up 5 m outside of the drilled plot perimeter along the four sides of plots 3 and 4 to monitor dust over a period of approximately 20 h after completion of drilling. Each dish contained 75 mL glycerol/ultra-pure water (50:50 v/v). Samples were covered with lids and collected after drilling. Samples were always collected from lowest presumptive concentration to greatest. To measure drift of dust during loading of the hoppers on the seeder, Petri-dishes were set up in rows of 10 at 1, 3, 5, 10 & 20 m downwind from the seeder. Dishes were filled with 75 mL glycerol/ultra-pure water (50:50 v/v).  	**4**



After deposition, Petri-dish samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. All samples were transported un-chilled to the Syngenta facility in Tiercé where they were then stored in freezers (≤-18). Field recovery samples held open upwind of the drilling were treated in the same way. Samples were shipped frozen to eurofins-ADME Bioanalyses for analysis and were analyzed within two months of arrival.

The glycerol-water solution was analyzed directly with a high-performance liquid chromatography with mass spectrometry detection (LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard for TMX was 99.7% pure and that for clothianidin 98%. The LOQ for the Petri-dish collectors was 0.001 µg/dish. Recovery for the Petri-dish samples ranged from 91 to 99% with RSDs from 7 to 10% for TMX and 91 to 96% (RSD 6-11%) for clothianidin. Recovery for the field spikes was 87% for TMX and 90% for clothianidin (Table 13).

	Raw residue data were converted from percent of application rate (71.6 g/ha) to g/ha for comparison to the NOAER. The greatest mean deposition at any distance from the zero line was used to calculate the trial mean. Clothianidin was not detected above the LOQ in any deposition sample but was found in small amounts in dust-filters attached to the seeder (not included in the WoE).		
Use of GLP and QA/QC	This was a GLP study with QA and QC.		**4**
Transparency of data	All raw data were provided.		**4**
Number of samples and replication	The study was conducted at two sites with one replicate.		**2**
Duration of study sufficient to observe trends	Duration was appropriate for the objectives of the study.		**4**
Overall evaluation of methods	Computed mean of above		**3.6**
Score for expert judgment on Quality of the study.		**1**	**3.60**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (Tables 15-34).

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Seeder with Syngenta deflector	Max mean value at 3 & 5 m distance from the zero line (n = 20)	0.07	0.67	0.1
Seeder with Syngenta deflector start and end	Max mean value at 3 & 5 m distance from the zero line (n = 20)	0.05	0.49	0.1
Seeder with Monosem deflector	Max mean value at 3 m distance from the zero line (n = 20)	0.04	0.35	0.1
Seeder with Monosem deflector start and end	Max mean value at 3 & 5 m distance from the zero line (n = 20)	0.04	0.40	0.1
Remobilization from soil	Max mean value at 5 m distance (n = 20)	0.00	0.00	0.1
Filling seed hoppers	Max mean value at 1 m distance from the zero line (n = 20)	0.92	9.22	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 and 5 m from the zero-line seeded with a seeder with a Syngenta deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 and 5 m from the zero-line at the ends of the field seeded with a seeder with a Syngenta deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 m from the zero-line seeded with a seeder with a Monosem deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 and 5 m from the zero-line at the ends of the field seeded with a seeder with a Monosem deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 5: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited because of remobilization at 5 m from the zero line of the field seeded with a seeder with a deflector resulted in exposures that were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 6: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited 1 m from the seeder during loading of the hoppers were >NOAER for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

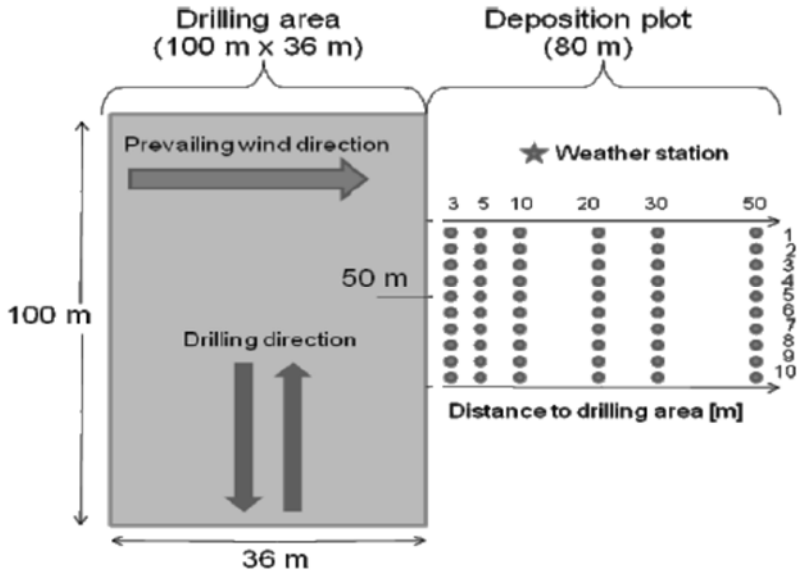
Expert judgment		
QA	Yes	May 27, 2016
SEJ	Yes	May 29, 2016

Narrative

Loading of seed hoppers is also a potential source of exposures to dust. Clothianidin was not detected above the LOQ in any deposition sample.

(Syngenta 2010e)
Report: Syngenta. 2010. Thiamethoxam – Investigating the Deposition of Dust from Pneumatic Drilling of A9700B Treated Maize Seeds in Italy During 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_11508-A9700BS. 72 p

This study was conducted to evaluate drift of dust resulting from the seeding of maize treated with TMX with a pneumatic driller. Deposition samples were collected downwind of the driller.

Responses 1-2: Quality of methods		Score
Experimental design and hypotheses	The study was carried out at two locations in the Porto Tolle, Veneto, Italy. The seeded plots were 3.6 ha and there were two sites. Seeding was done on 2009-07-08. Site 2 was planted to beet seeds treated with TMX 5 months prior to the study but the crop failed. This invalidated the GLP study on maize (due to soil residues of TMX and clothianidin of 0.019 mg/kg and 0.005 mg/kg, resp.), but the data were included in the WoE as this scenario is possible under real-world conditions. The var. of the treated maize seed was NK Famoso. Seeds were treated with Celest XL/Cruiser 350 FS. Concentration on the seeds was measured at 0.62 mg TMX/seed. The driller was a Gaspardo MT8 fitted with a Syngenta model deflector and seeds were drilled at 95,791 seeds/ha (59.4 g a.i./ha) and 96,117 seeds/ha (59.6 g a.i./ha) on Fields 1 & 2, resp. Mean wind speeds varied between 1.5 and 3.9 m/sec during drilling (Appendix 1.19 & 1.23). Weather and wind conditions were recorded during drilling (Appendix 1.19, 1.20, 1.23, & 1.24). Mean application rate was 59.5 g TMX/ha on all plots. Six rows of ten Petri-dishes (143.14 cm^2) were set up downwind of the test plot at distances of 3, 5, 10, 20, 30, and 50 m from the zero line (see diagram below). Each dish contained 75 mL glycerol/ultra-pure water (50:50 v/v). Samples were covered with lids and collected after drilling. 	4

	After deposition (32 and 31 min after completion of drilling), Petri-dish samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. All samples were frozen at ≤-18 within 8 h of collection. Field recovery samples held open upwind of the drilling were treated in the same way. Samples were shipped frozen to eurofins-ADME Bioanalyses for analysis. The glycerol-water solution was analyzed directly with a high-performance liquid chromatography with mass spectrometry detection (LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard for TMX was 99.7% pure and that for clothianidin 98%. The LOQ for the Petri-dish collectors was 0.001 µg/dish. Recovery for the Petri-dish samples ranged from 91 to 100% with RSDs from 4.7 to 12.7% for TMX and 90 to 99% (RSD 3.8-13.9%) for clothianidin (Appendix 5). Recovery for the field spikes was 93% for TMX and 92% for clothianidin (Section 4.5). Raw residue data were converted from percent of application rate (59.5 g) to g/ha for comparison to the NOAER. The greatest mean deposition at any distance from the zero line was used to calculate the trial mean. Clothianidin was not detected above the LOQ in any deposition sample.	
Use of GLP and QA/QC	This was a GLP study with QA and QC.	**4**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	The study was conducted at two sites with one replicate.	**2**
Duration of study sufficient to observe trends	Duration was appropriate for the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.6**
Score for expert judgment on Quality of the study.	**1**	**3.60**

Relevance

Deposition of TMX at distances away from the seeding operation with maize seeds treated with TMX (Section 4.4 and Appendix 7).

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Field Site 1	Max mean value at 10 m distance from the zero line (n = 10)	0.02	0.24	0.1
Field Site 2	Max mean value at 3 m distance from the zero line (n = 10)	0.33	3.33	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects		Score
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 10 m from the zero-line seeded with a seeder with a Syngenta deflector resulted in exposures that were <NOAER for honeybees.	**0**

Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The concentrations of TMX deposited at 3 m from the zero-line treated with TMX 5 months prior to the tests and seeded with TMX-treated maize seed with a seeder with a Syngenta deflector resulted in exposures that were >NOAER for honeybees.		**4**
Overall evaluation relevance	Computed mean of above score(s)		**4.00**
Score for expert judgment on relevance of the results.		**1**	**4.00**

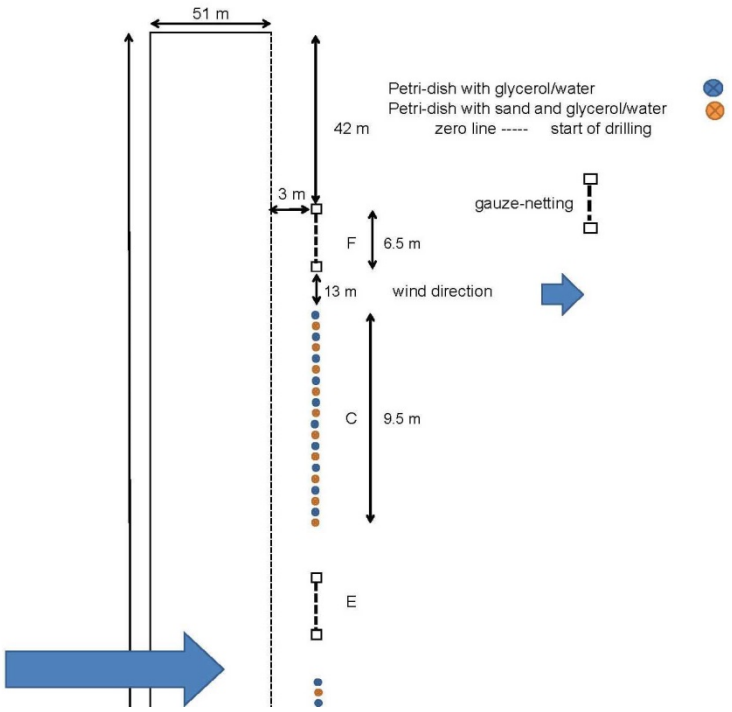
Expert judgment		
QA	Yes	May 27, 2016
SEJ	Yes	May 29, 2016

Narrative.
The greater deposition at Site 2 suggests that the residue of TMX in soil 19 ng/g soil may have resulted in significant contamination from soil dust disturbed during seeding or from human activity during collection of the dishes. This double-treatment scenario might occur in agricultural practices so is potentially realistic. Visual inspection of the dishes during collection might have provided confirmation of this route of contamination.

(Syngenta 2011c)
Report: Syngenta. 2011. Investigating the Dust Deposition during Sowing of Seed-Treated Oilseed Rape Seeds with Air Assisted (Pneumatic) Sowing Machinery. Frankfurt am Main, Germany: Syngenta Ltd. (Unpublished Report). Report A9807C_10977 - CWFG - A9807C. 122 p

The objective of the study was to establish the drift pattern of dust emitted from an air-assisted pneumatic drilling machine during sowing of TMX-treated oilseed rape seed. This study measured the deposition of TMX at soil level using Petri-dish collectors with a liquid matrix and wet-sand matrix. In addition, gauze netting samplers were deployed. The latter are three-dimensional gauze samplers for which appropriate toxicity data are not available; these were not included in the WoE.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	This study was conducted on 2010-10-28. The study was conducted in Ubstadt-Stettfeld, Baden-Württemberg, Germany. The field was 1 ha in area. The history of cropping and pesticide use in the field were provided (Section 6.2 and Table 4) and TMX had not been used in the previous three years. There was one site and one replicate. The oilseed rape seeds (var. Baldur) were treated with a formulation of TMX (Batch ID ST51BN/MA). The measured amount of a.s. on the seeds was 4.49 g TMX/kg seeds. Seeding was conducted with an Accord DA seeder at a measured rate of 727,273 seeds/ha. Weather conditions were recorded (Table 5) and the mean wind speed during drilling ranged from 2.43 to 5.34 m/sec (Table 8). The final application rate was 17.96 g/ha. Samplers were set up as indicated below: There were three replicated rows of 20 Petri-dishes (143.14 cm^2; in three different locations, A, B, and C) arranged three m from the zero line on the downwind side (see partial diagram below). Alternating dishes were filled either with 75 mL glycerol/ultra-pure water (50:50 v/v) or 50 g of quartz sand and 17 mL of glycerol/ultra-pure water (50:50, v/v) to provide 10 each in the row in three locations. Gauze net samplers sprayed with glycerol/ultra-pure water (50:50, v/v) were deployed but were not included in the WoE. After drilling (30 min), Petri-dishes were covered with lids and collected. After collection, liquid-matrix Petri-dish samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. All samples were frozen at ≤-18 within 2.5 h of collection. For the sand-matrix dishes, most of the samples were frozen as is and then transferred later and without thawing transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. It is not clear whether field recovery samples were used (*weakness*). Samples were shipped frozen to Eurofins Agroscience Services Chem GmbH for analysis. The glycerol-water solutions and the sand-matrix solutions were analyzed using standard methods. Quantification was with high performance liquid chromatography with mass spectrometry detection (LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard for TMX was 99.7% pure and that for clothianidin 98%. The LOQ for the Petri-dish collectors was 0.001 µg/dish. Mean recovery of TMX for the liquid Petri-dish samples was	**3**

	93% with RSD of 6.6% and from the sand-matrix dishes was 93(4.7%). For clothianidin, mean recovery was and 92(5.8%) for the liquid samples and 97(3.5%) (p 68). Raw residue data were provided in mg TMX/ha and were converted to g/ha for comparison to the NOAER. Clothianidin was not detected above the LOQ in any petri dish deposition sample.  	
Use of GLP and QA/QC	The study was full GLP with QA and QC.	**4**
Transparency of data	All raw data were provided	**4**
Number of samples and replication	There was one site and one replicate. Multiple samples in the site were pseudoreplicated.	**1**
Duration of study sufficient to observe trends	The duration of the study was appropriate to the objectives.	**4**
Overall evaluation of methods	Computed mean of above	**3.2**
Score for expert judgment on Quality of the study.	**1**	**3.20**

Relevance

Deposition of TMX at 3 m away from the seeding operation with oilseed rape seeds treated with TMX (Table 15 & 16)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Liquid matrix collectors	90th centile 3 m distance from the zero line (n = 30)	0.0029	0.03	0.1

Deposition of TMX at 3 m away from the seeding operation with oilseed rape seeds treated with TMX (Table 15 & 16)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Sand matrix collectors	90th centile 3 m distance from the zero line (n = 30)	0.0021	0.02	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in liquid and sand-matrix collectors at 3 m distance from the zero line were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

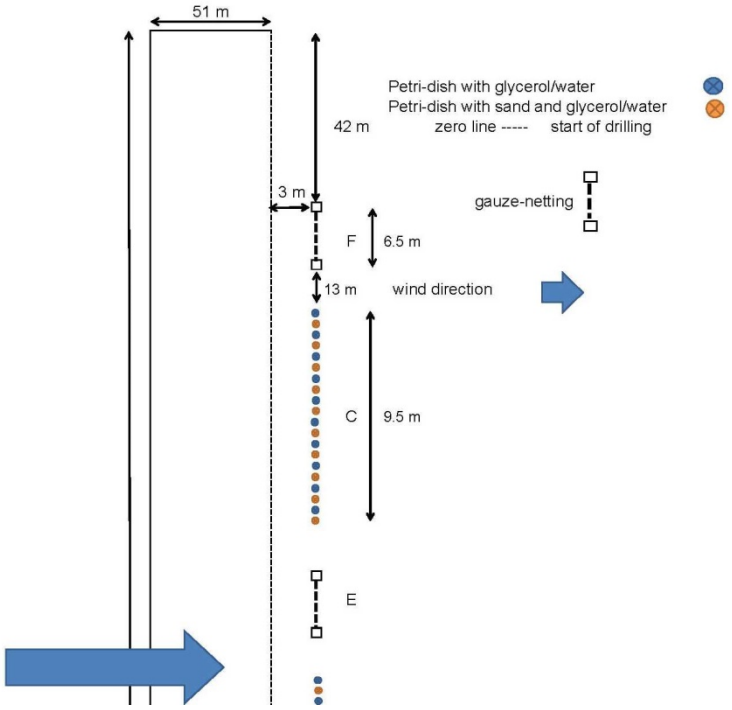
Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 30, 2016

Narrative.
By t-test there were no significant differences between the means of the liquid and the sand collectors.

(Syngenta 2011a)
Report: Syngenta. 2011. Investigating the Dust Deposition during Sowing of Seed-Treated Oilseed Rape Seeds with Air Assisted (Pneumatic) Sowing Machinery. Frankfurt am Main, Germany: Syngenta Ltd. (Unpublished Report). Report A9807C_10978 - CWFG - A9807C. 61 p

The objective of the study was to establish the drift pattern of dust emitted from an air-assisted pneumatic drilling machine during sowing of TMX-treated oilseed rape seed. This study measured the deposition of TMX at soil level using Petri-dish collectors with a liquid matrix and wet-sand matrix. In addition, gauze netting samplers were deployed. The latter are three-dimensional gauze samplers for which appropriate toxicity data are not available; these were not included in the WoE.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	This study was conducted on 2011-04-15. The study was conducted in vicinity of Pforzheim (Baden-Württemberg), Germany. The field was 1 ha in area. The history of cropping and pesticide use in the field was provided (Section 6.2 and Table 3) and TMX had not been used in the previous three years. There was one site and one replicate. The oilseed rape seeds (var. Taurus) were treated with a formulation of TMX (D/KI 9147962 A ST51Bn/MB). The measured amount of a.s. on the seeds was 4.56 g TMX/kg seeds. Seeding was conducted with a Kuhn Combiliner Venta LC302 seeder at a measured rate of 944,930 seeds/ha. Weather conditions were recorded (Table 4) and the mean wind speed during drilling ranged from 2.69 m/s to 4.64 m/sec (Table 7). The final application rate was 26.72 g TMX/ha. Samplers were set up as indicated below: there were three replicated rows of 20 Petri-dishes (143.14 cm^2; in three different locations, A, B, and C) arranged three m from the edge of the field on the downwind side (see partial diagram below). Alternating dishes were filled either with 75 mL glycerol/ultra-pure water (50:50 v/v) or 50 g of quartz sand and 17 mL of glycerol/ultra-pure water (50:50, v/v) to provide 10 each in the three locations. Gauze net samplers sprayed with glycerol/ultra-pure water (50:50, v/v) were deployed but were not included in the WoE. After drilling (30 min), Petri-dishes were covered with lids and collected. After collection, liquid-matrix Petri-dish samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. All samples were frozen at ≤-18 within 2 h of collection. For the sand-matrix dishes, the samples were frozen as is and then transferred later and without thawing to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. It is not clear whether field recovery samples were used (*weakness*). Samples were shipped frozen to Eurofins Agroscience Services Chem GmbH for analysis. The glycerol-water solutions and the sand-matrix solutions were analyzed using standard methods. Details of the analytical methods	**2**

	were not provided in the report (*weakness*) but were assumed to be the same as those in a related study[24]. Raw residue data were provided in mg TMX/ha and were converted to g/h for comparison to the NOAER. Clothianidin was not detected above the LOQ in any petri dish deposition sample.  	
Use of GLP and QA/QC	The study was full GLP with QA and QC.	**4**
Transparency of data	All raw data were provided	**4**
Number of samples and replication	There was one site and one replicate. Multiple samples in the site were pseudoreplicated.	**1**
Duration of study sufficient to observe trends	The duration of the study was appropriate to the objectives.	**4**
Overall evaluation of methods	Computed mean of above	**3**
Score for expert judgment on Quality of the study.	**1**	**3.00**

[24] Syngenta. 2011. Investigating the Dust Deposition during Sowing of Seed-Treated Oilseed Rape Seeds with Air Assisted (Pneumatic) Sowing Machinery. Frankfurt am Main, Germany: Syngenta Ltd. (Unpublished Report). Report A9807C_10977 - CWFG - A9807C. 122 p

Relevance

Deposition of TMX at 3 m away from the seeding operation with oilseed rape seeds treated with TMX (Table 14 & 15)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Liquid matrix collectors	90th centile 3 m distance from the zero line (n = 30)	0.0098	0.002	5
Sand matrix collectors	90th centile 3 m distance from the zero line (n = 30)	0.0156	0.003	5

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			Score
Comparison of exposure value to toxicity value	The concentrations of TMX measured in liquid and sand-matrix collectors at 3 m distance from the zero line were <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

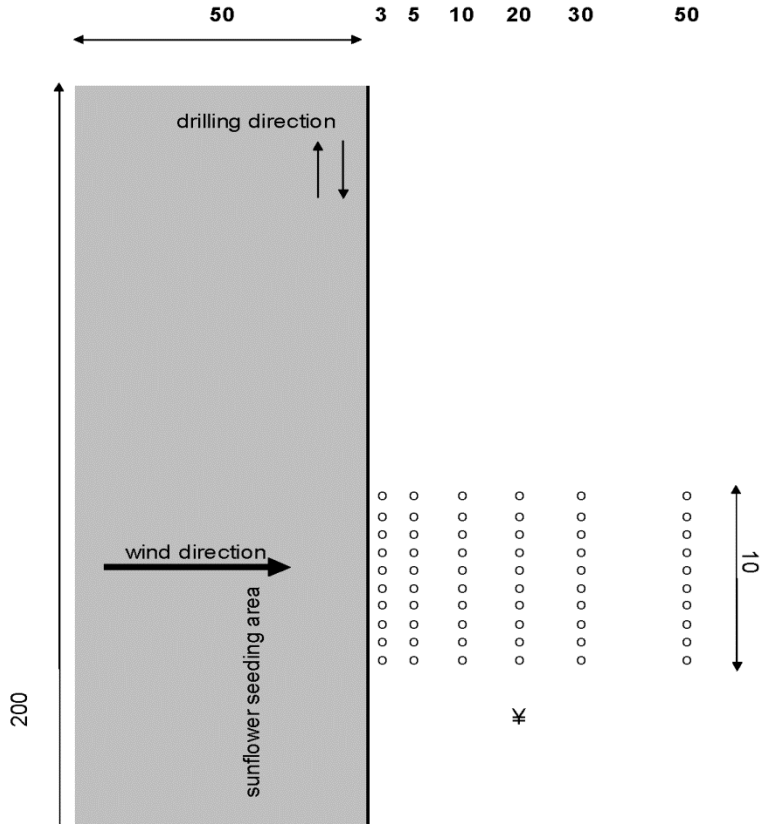
Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 30, 2016

Narrative.
By t-test there was a significant difference ($p < 0.05$) between the means of the liquid and the sand collectors. The mean value for the liquid matrix was 0.0068 vs. 0.0114 g TMX/ha.

(Syngenta 2012c)
Report: Syngenta. 2012. Thiamethoxam - Investigating the Deposition of Dust from Pneumatic Drilling of A9700B Treated Sunflower Seeds in Northern Germany During 2011. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10950 - A9700B. 115 p

The objective of the study was to measure the deposition of TMX and clothianidin in dust generated during seeding of TMX-treated sunflower seed with deflector-modified pneumatic drilling machine under field conditions. Samples of dust from filters attached to driller fan exhaust were measured in a separate trial but not included in the WoE.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	This study was conducted at two sites on 2011-09-30 and 2011-10-17. The study was conducted in Kutenholz/Mulsum in the vicinity of Stade (Northern Germany). The history of cropping and pesticide use in the field was provided (Tables 3-6) and TMX had not been used in the previous three years. There were two sites and one replicate. The plot at site-1 was 1.08 ha and the total at site-2 was 2.31 ha, but only 1.08 ha was drilled for the petri-dish trial. The sunflower seeds (var. Alexandra PR) were treated with a formulation of TMX (Cruiser 350 FS). The measured amount of a.s. on the seeds was 3.799 g TMX/kg seeds. Seeding was conducted with Kuhn Maxima (8 hoppers) low pressure pneumatic seed driller with a seeding rate of 84,367 seeds/ha for site-1 and 83,493 for site-2 and deflectors. Weather conditions were recorded (Tables 8 and 9) and the mean wind speed during drilling ranged from 1.97 to 3.85 m/sec for site-1 and 2.89 to 4.56 m/sec (Tables 11 & 14). The final application rates were 22.03 and 21.81 g/ha, resp. Samplers were set up as indicated below: There were six rows of 10 Petri-dishes (143.14 cm^2) filled with 75 mL glycerol/ultra-pure water (50:50 v/v) set up at 3, 5, 10, 20, 30, and 50 m from the zero line. After drilling (30 min), Petri-dishes were covered with lids and collected. After collection, Petri-dish samples were transferred to 250-ml polypropylene bottles with the aid of rinses of ultrapure water. All samples were frozen at ≤-18 within 5 and 6 h of collection for sites 1 and 2, resp. Field recovery samples were used. Samples were shipped frozen to Eurofins Agroscience Services Chem GmbH in Germany for analysis. The deposition samples were analyzed using standard methods (GRM009.05A). Quantification was with high performance liquid chromatography with mass spectrometry detection (LC-MS/MS). Isotopically labeled internal standards were not used but the reference standard for TMX was 99.7% pure and that for clothianidin 98% (p 73). The LOQ for the Petri-dish collectors was 0.001 µg/dish. Mean recovery of TMX was 94(15%) (p. 82). For clothianidin, mean recovery was 92(15%) (p 83). Recovery for the field spikes was 82% for TMX and 84% for clothianidin (Table 28).	**4**

	 Raw residue data were provided and 90th centiles were calculated in % of field rate. These were converted to g/ha for comparison to the NOAER. Clothianidin was detected above the LOQ in only one deposition sample.	
Use of GLP and QA/QC	The study was full GLP with QS and QC.	**4**
Transparency of data	All raw data were provided	**4**
Number of samples and replication	There were two sites and one replicate. Multiple samples in each site were pseudoreplicated.	**1**
Duration of study sufficient to observe trends	The duration of the study was appropriate to the objectives.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Deposition of TMX at various distances away from the seeding operation with sunflower seeds treated with TMX in Germany (Table 26)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Site-1, pneumatic seeding with deflector	90th centile for all distances from the zero line	0.0225	0.22	0.1

Site-2, pneumatic seeding with deflector	90th centile for all distances from the zero line	0.0249	0.25	0.1

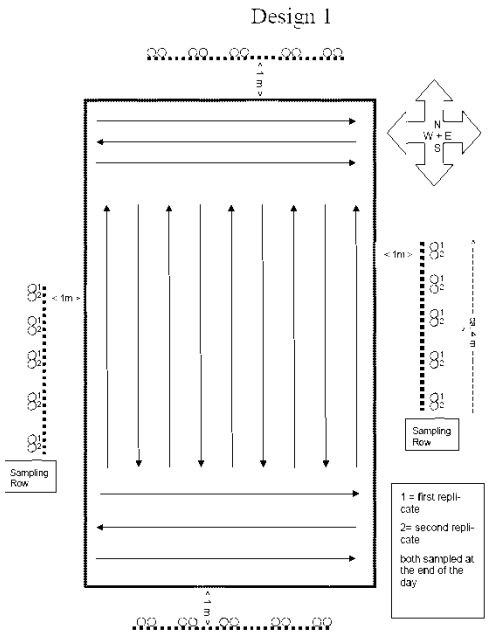
Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table. Green cells indicate no relevant exposure.

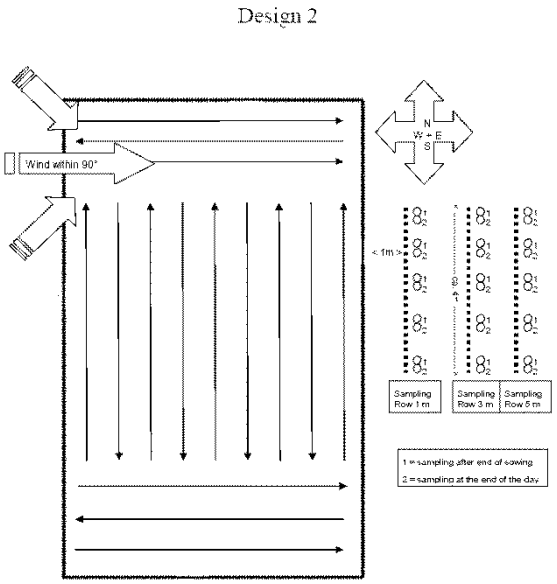
Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX deposited from pneumatic sowing at all distances from the zero line at site-1 and site-2 was <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2012e)
Report: Syngenta. 2012. Thiamethoxam and CGA322704 - A9807C - Monitoring of the Deposition of Thiamethoxam and CGA322704 Dust Emitted During Sowing of Oil-Seed Rape Dressed with Cruiser OSR (Germany, 2008). Maintal, Germany: Syngenta Ltd. (Unpublished Report). Report A9807C_10980 - A9807C. 58 p

The purpose of this study was to monitor the levels of TMX and clothianidin under field conditions during sowing of oil-seed rape seeds treated with CRUISER™ OSR. Mechanical and pneumatic seeders were used in the studies.

Responses 1-4: Quality of methods		Score
Experimental design and hypotheses	Twenty test sites, managed by experienced professional farmers, were selected in main oil-seed rape growing areas across Germany. These sites represented different climatic, soil and farm sizes. The farmers were asked to follow normal sowing practice, typically for the growing area (Table 1 to Table 4). The study was started on 2008-08-16 and was completed on 2008-09-01. Seeds were treated at Syngenta (Syngenta Seeds GmbH, Bad Salzuflen) with commercial batches of CRUISER™ OSR (280 g/L TMX, 32 g/L metalaxyl-M, and 8 g/L fludioxonil) except for the seeds used on site 17, which were treated with ELADO™ containing clothianidin (these data were omitted from the WoE). The seeder was filled with treated seeds at a place distant from the test field to avoid contamination of the site before the onset of sowing. Conditions of sowing were provided (Tables 2-4). Type of seeder was recorded (Table 3) and the make of seeder varied. Use of deflectors was not reported. Before sowing, Petri-dishes containing 50 ml of a mixture (50/50) of water and glycerol were set up adjacent to the test field. Depending on the wind situation, two different experimental set-ups were possible: 1) In situations of an unclear or variable wind direction, one row of Petri-dishes was placed at approximately the center of each of the four sides of the test field, in 1 m distance from the outer sowing row (Design 1); and, 2) When a clear wind direction could be discerned, three rows of Petri-dishes were placed at approximately the center of the downwind side of the field at 1, 3, and 5 m from the outer sowing row (Design 2). Each row consisted of 10 Petri-dishes (143.14 cm^2), set up in five pairs of two. Wherever feasible (depending on weather conditions, time of sowing, logistical constraints etc.) 5 of these 10 dishes (1 from each pair) were sampled commencing ca. 5 minutes after sowing had ended (Sampling  	3

	time 1), and the remaining 5 dishes were sampled by the end of the day (Sampling time point 2). On sites where this duplicate sampling was not possible, the two arrays of 5 dishes each were sampled simultaneously. The use of field spikes was not reported (*weakness*). The sampling liquids from the array of five (or ten) Petri-dishes were collected into light-proof bottles with the aid of five rinses of 10-20 ml of water each. Samples were transported from the field and placed in a freezer within 6-12 h of sampling. Samples were stored at or below a nominal temperature of -18°C until transported in a deep freeze vehicle to the analytical laboratory SGS Institut Fresenius in Taunusstein where they were kept frozen until preparation for analysis started.  Analysis followed standard methods. Isotopically labeled internal standards were not used but the reference standard for TMX was 99.7% pure and that for clothianidin 98%. The LOQ for the Petri-dish collectors ranged from 0.00051 to 0.00075 µg/dish. Mean recovery (RSD) of TMX was 98 (6.5%). For clothianidin, mean recovery was 99 (5%) (Table 6). Raw data were provided and medians and 90th centiles were calculated but only for % of applied. In some cases, the actual rate of application of TMX/ha was not known (*weakness*) and a default value of 12.6 g TMX/ha was assumed. In others, it varied from 8.6 to 34.1 g TMX/ha. Normalization to application rate was not possible in all cases (*potential weakness*) but assumption of a smaller application rate was conservative. For this WoE, the rate of deposition in mg/ha was used to calculate 90th centiles.	
Use of GLP and QA/QC	This study was not conducted under GLP but the protocol was clearly described.	**2**
Transparency of data	All raw data were provided.	**4**
Number of samples and replication	There were 20 sites each with one replicate.	**4**
Duration of study sufficient to observe trends	The duration was appropriate to the objectives of the study.	**4**
Overall evaluation of methods	Computed mean of above	**3.4**
Score for expert judgment on Quality of the study.	**1**	**3.40**

Relevance

Deposition of TMX at various distances away from the seeding operation with oilseed rape seeds treated with TMX in Germany (Tables 7-10)

Source of sample	Sample	TMX deposited in g/ha	Ratio of deposited rate to NOAER	Field rate equivalent to NOAER g/ha
Pneumatic sowing & variable wind direction (all with simultaneous sampling)	90th centile for all 4 sides at 1 m from the outer sowing row (n = 32)	0.0027	0.03	0.1
Pneumatic sowing & clear wind direction; simultaneous sampling	90th centile for all distances from the outer sowing row (n = 30)	0.0032	0.03	0.1
Pneumatic sowing & clear wind direction; consecutive sampling	90th centile for all distances from the outer sowing row (n = 42)	0.0052	0.05	0.1
Mechanical sowing & clear wind direction (mixed sampling)	90th centile for all distances from the outer sowing row (n = 18)	0.0011	0.01	0.1

Values <LOQ were treated as zero. Where toxicity values were exceeded by exposure values, relevance is shown with yellow or orange highlight in the Table above. Green cells indicate no relevant exposure.

Response 1: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX deposited from pneumatic sowing & variable wind direction at 1 m distances from the outer sowing row of all 4 sides of the field was <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 2: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX deposited from pneumatic sowing clear wind direction and simultaneous sampling at all distances from the outer sowing row was <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 3: Relevance to adverse effects			**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX deposited from pneumatic sowing & clear wind direction and consecutive sampling at all distances from the outer sowing row was <NOAER for honeybees.		**0**
Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Response 4: Relevance to adverse effects		**Score**
Comparison of exposure value to toxicity value	The 90th centile concentration of TMX deposited from mechanical sowing & clear wind direction (mixed sampling) at all distances from the outer sowing row was <NOAER for honeybees.	**0**

Overall evaluation relevance	Computed mean of above score(s)		**0.00**
Score for expert judgment on relevance of the results.		**1**	**0.00**

Expert judgment		
QA	Yes	May 30, 2016
SEJ	Yes	May 30, 2016

Narrative

The 90th centile from the mechanical sowing was smaller than that for pneumatic but the means were not significantly different ($p > 0.05$ for t-test of untransformed data).

Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds

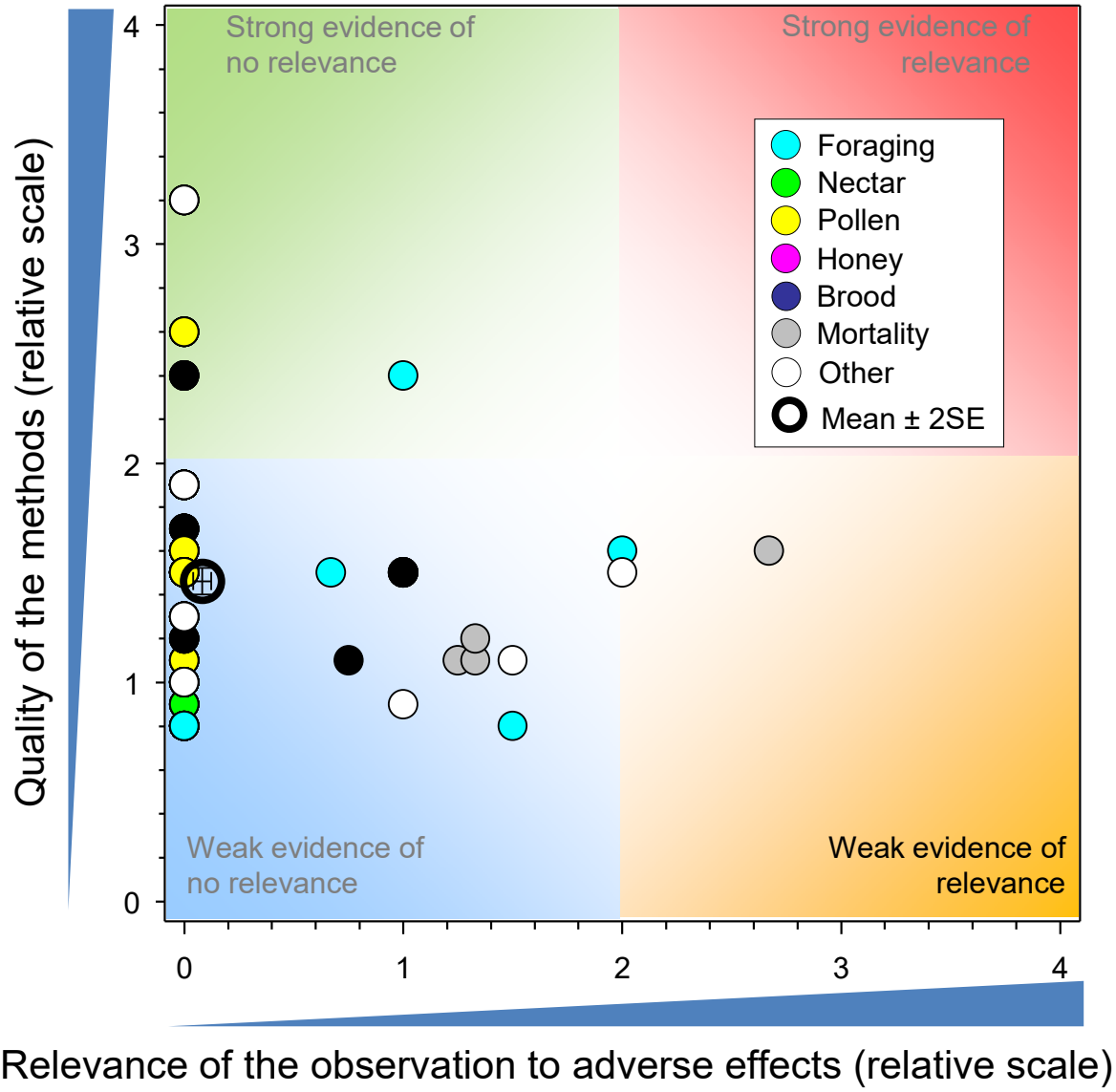
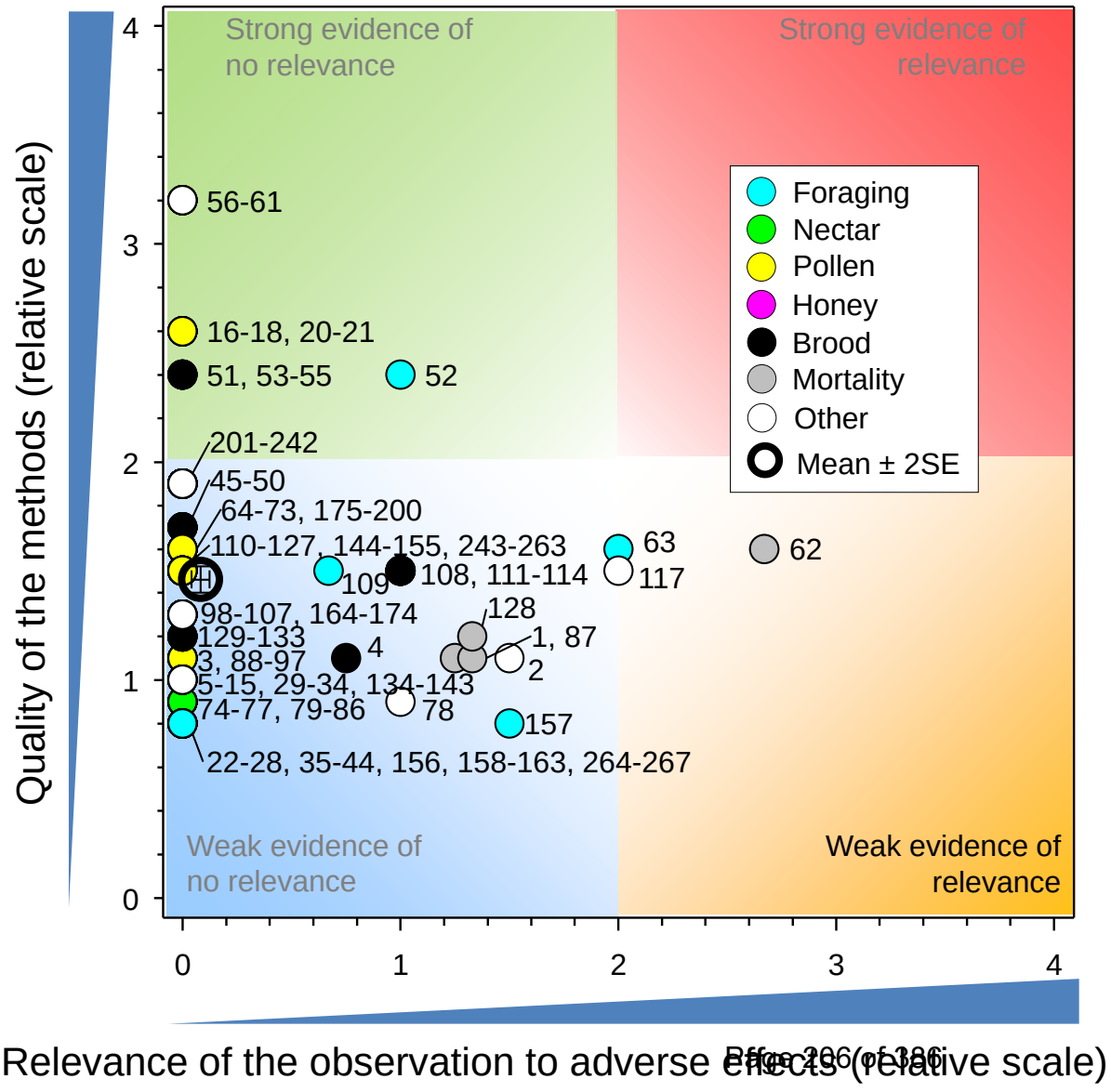


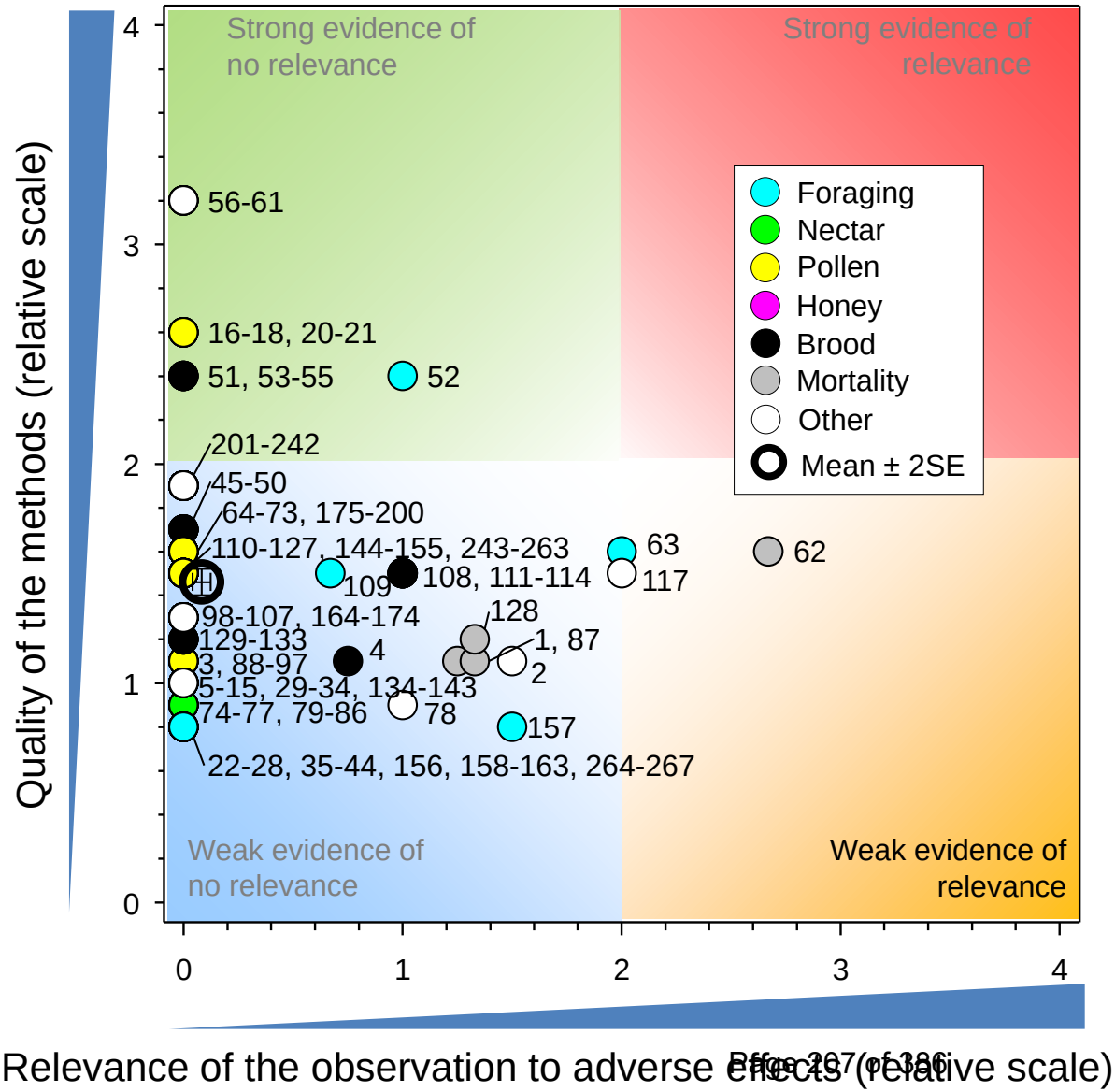
Figure 4. Quality and relevance of effects in honeybees exposed in controlled field studies via crops treated with TMX as seed dressings, n = 267. Symbols may obscure others, see this SI below for all responses. There were no points obscured by the legend.

Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



1 = (Henry et al. 2015) Resp 1
2 = (Henry et al. 2015) Resp 2
3 = (Henry et al. 2015) Resp 3
4 = (Henry et al. 2015) Resp 4
5 = (Pilling et al. 2013) Resp 1
6 = (Pilling et al. 2013) Resp 2
7 = (Pilling et al. 2013) Resp 3
8 = (Pilling et al. 2013) Resp 4
9 = (Pilling et al. 2013) Resp 5
10 = (Pilling et al. 2013) Resp 6
11 = (Pilling et al. 2013) Resp 7
12 = (Pilling et al. 2013) Resp 8
13 = (Pilling et al. 2013) Resp 9
14 = (Pilling et al. 2013) Resp 10
15 = (Pilling et al. 2013) Resp 11
16 = (Pohorecka et al. 2012) Resp 1
17 = (Pohorecka et al. 2012) Resp 2
18 = (Pohorecka et al. 2012) Resp 3
19 = (Pohorecka et al. 2012) Resp 4
20 = (Pohorecka et al. 2012) Resp 5
21 = (Pohorecka et al. 2012) Resp 6
22 = (Syngenta 1998b) Resp 1
23 = (Syngenta 1998b) Resp 2
24 = (Syngenta 1998b) Resp 3
25 = (Syngenta 1998b) Resp 4

Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



26 = (Syngenta 1998b) Resp 5
27 = (Syngenta 1998b) Resp 6
28 = (Syngenta 1998b) Resp 7
29 = (Syngenta 1998a) Resp 1
30 = (Syngenta 1998a) Resp 2
31 = (Syngenta 1998a) Resp 3
32 = (Syngenta 1998a) Resp 4
33 = (Syngenta 1998a) Resp 5
34 = (Syngenta 1998a) Resp 6
35 = (Syngenta 1999) Resp 1
36 = (Syngenta 1999) Resp 2
37 = (Syngenta 1999) Resp 3
38 = (Syngenta 1999) Resp 4
39 = (Syngenta 1999) Resp 5
40 = (Syngenta 1999) Resp 6
41 = (Syngenta 1999) Resp 7
42 = (Syngenta 1999) Resp 8
43 = (Syngenta 1999) Resp 9
44 = (Syngenta 1999) Resp 10
45 = (Syngenta 2000b) Resp 1
46 = (Syngenta 2000b) Resp 2
47 = (Syngenta 2000b) Resp 3
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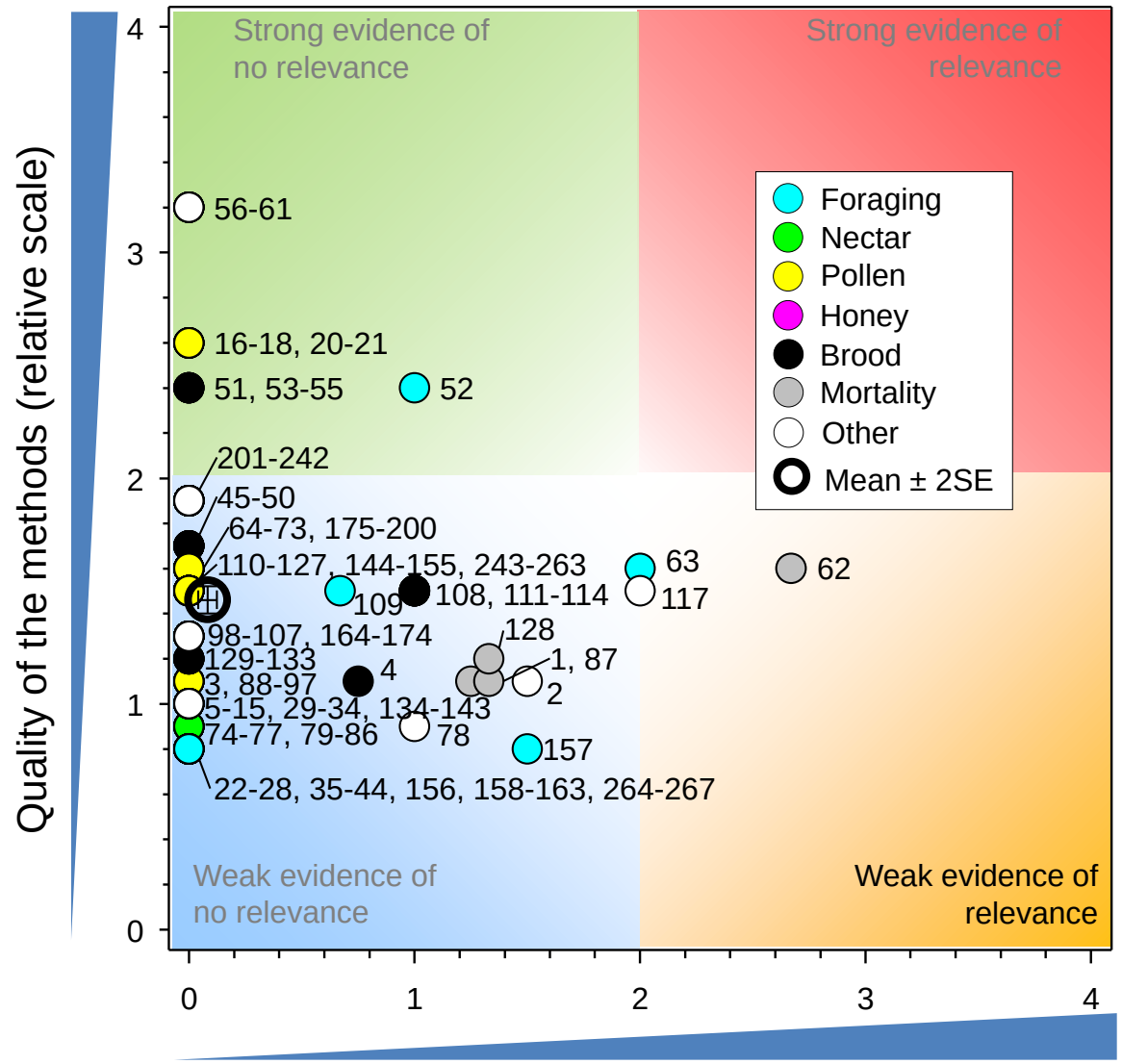
50 = (Syngenta 2000b) Resp 6

Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



51 = (Syngenta 2000g) Resp 1
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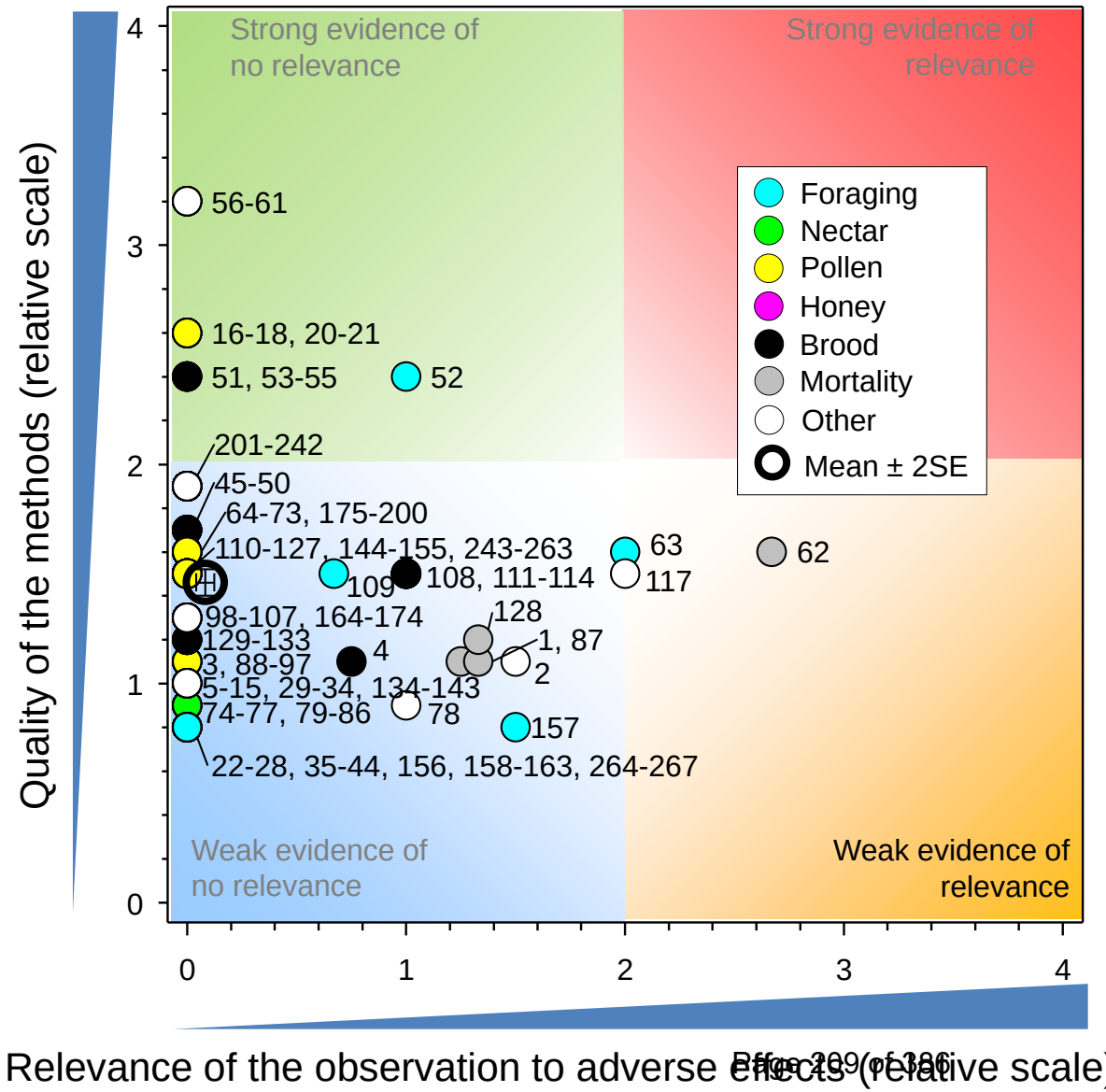
Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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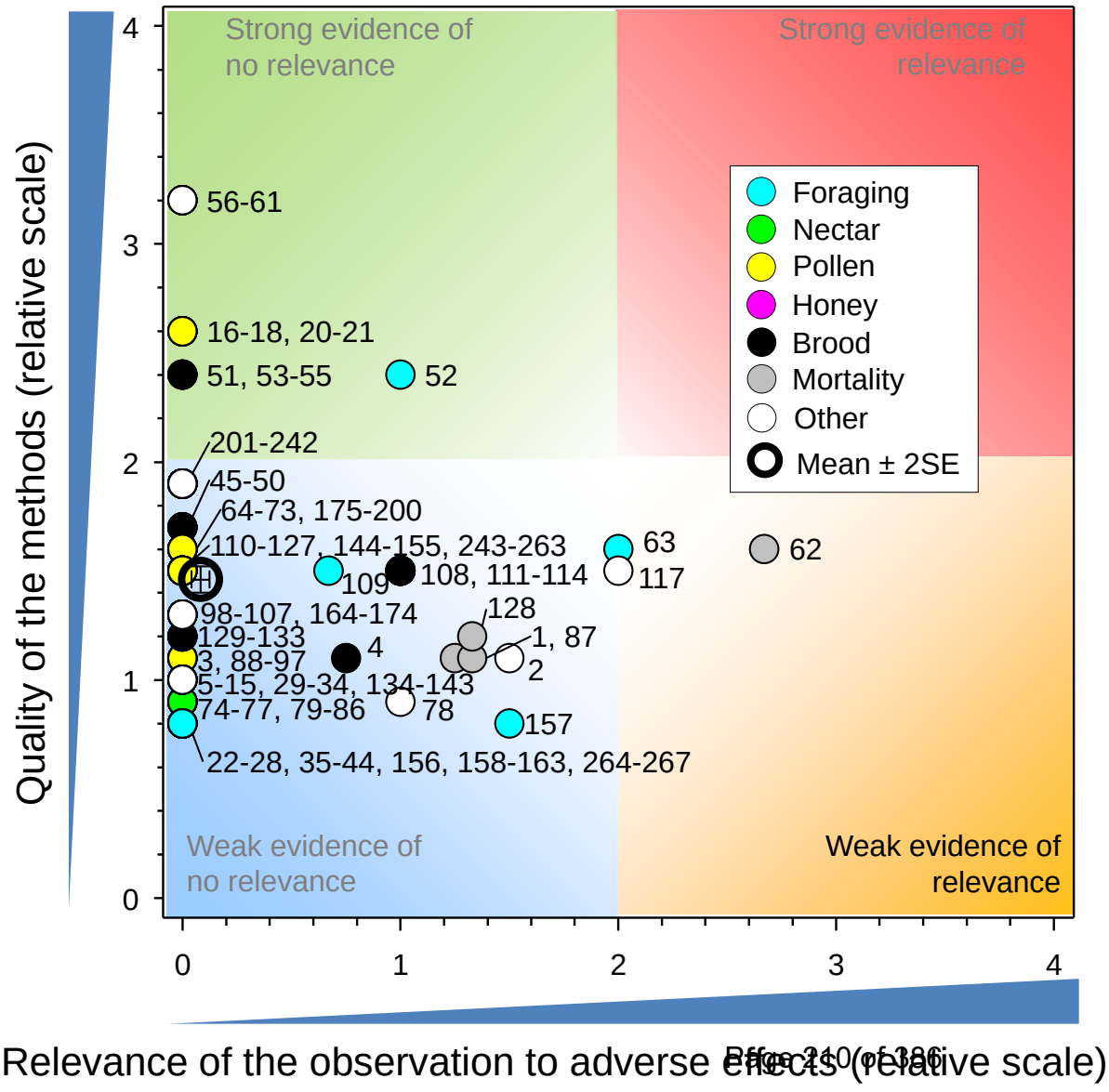
Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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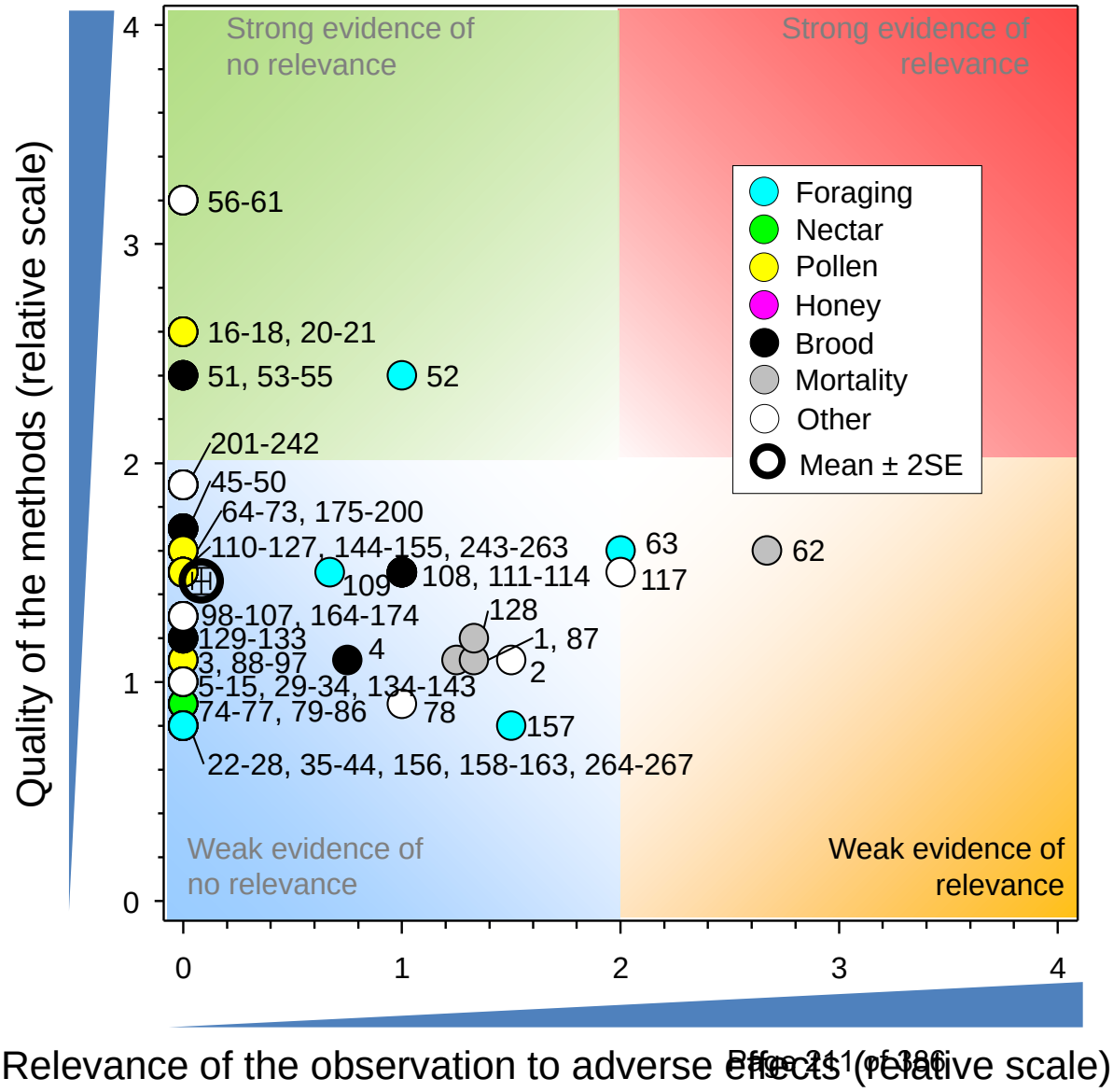
Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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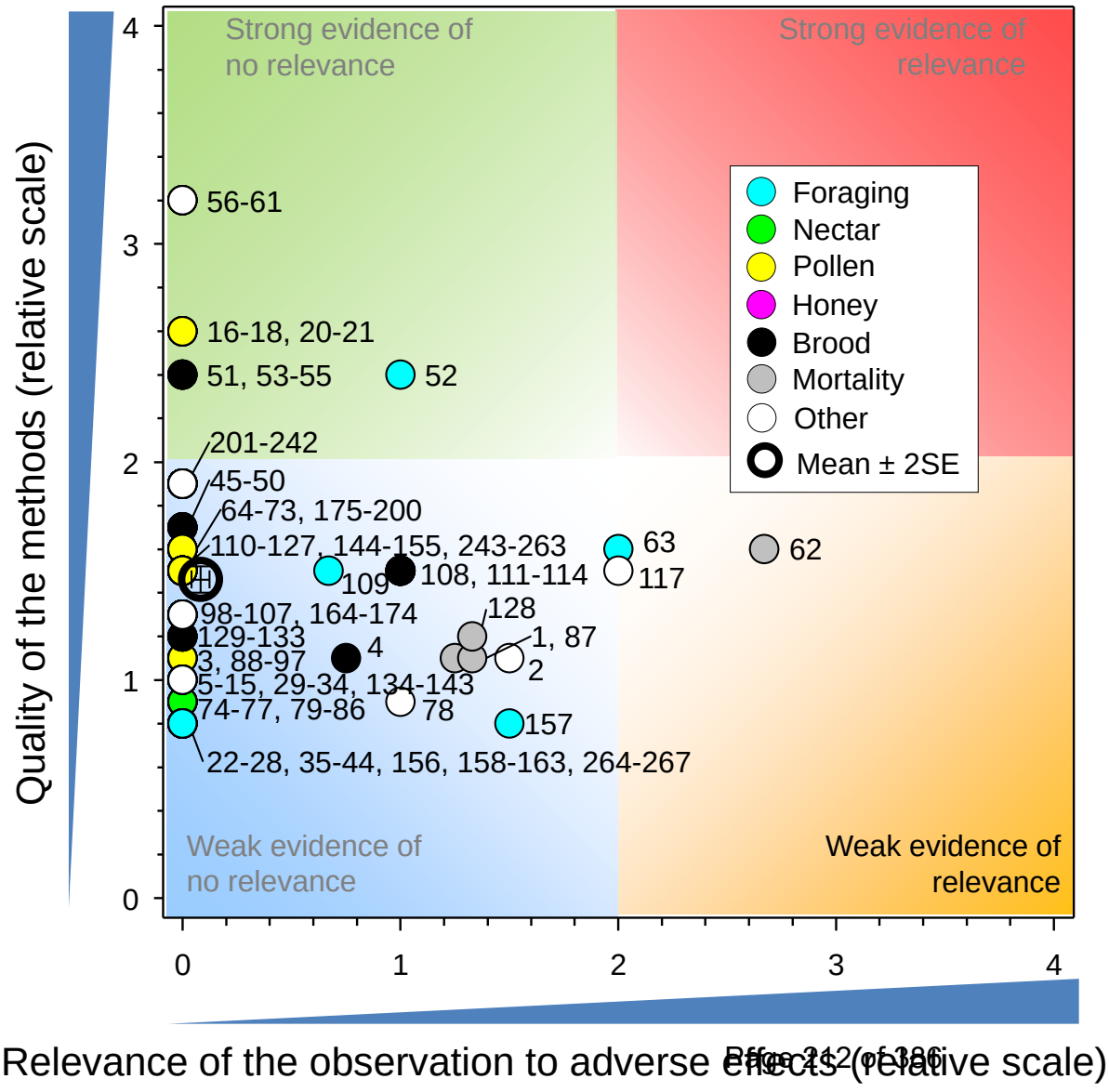
150 = (Syngenta 2001f) Resp 7

Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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166 = (Syngenta 2003b) Resp 3
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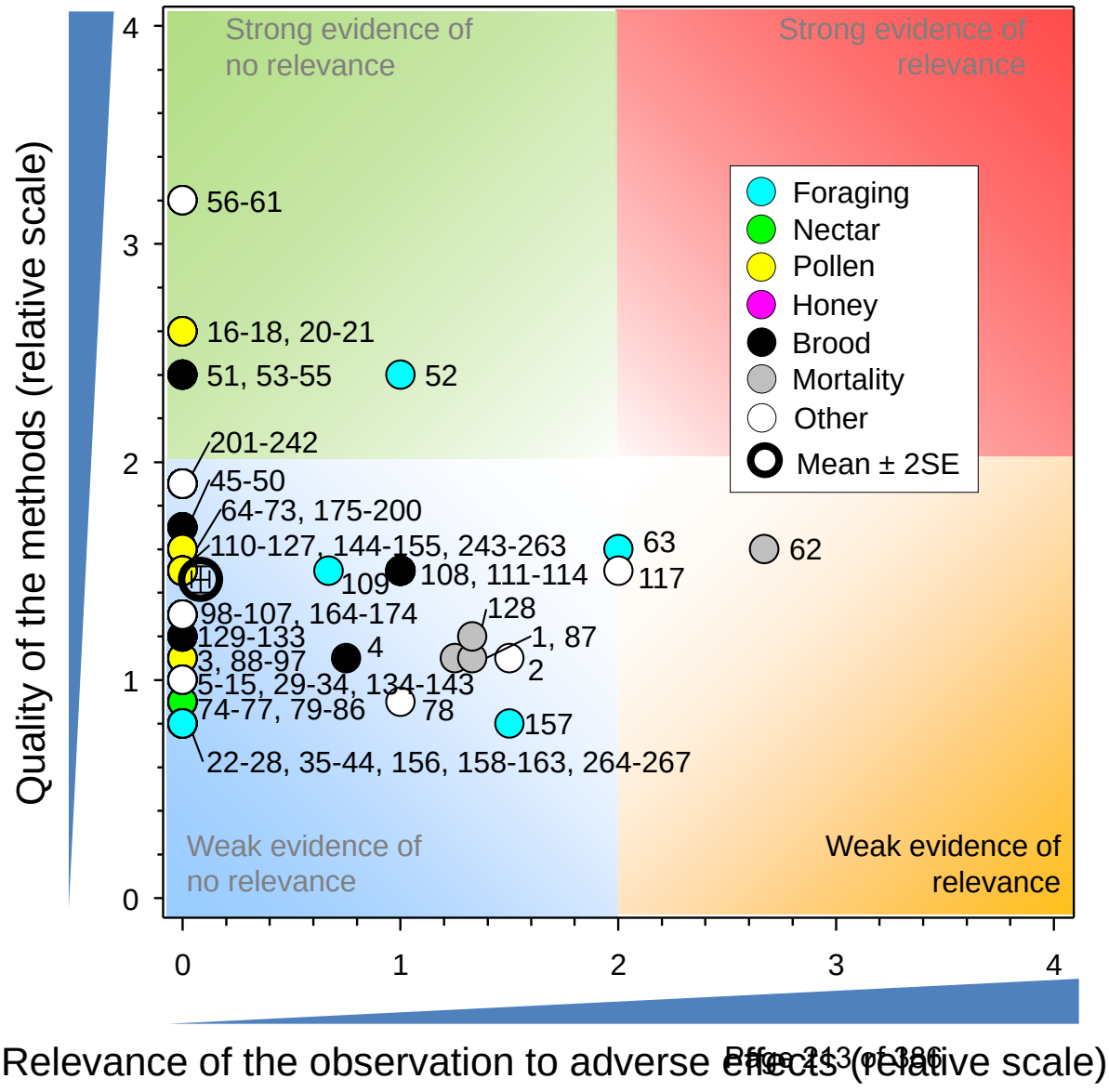
Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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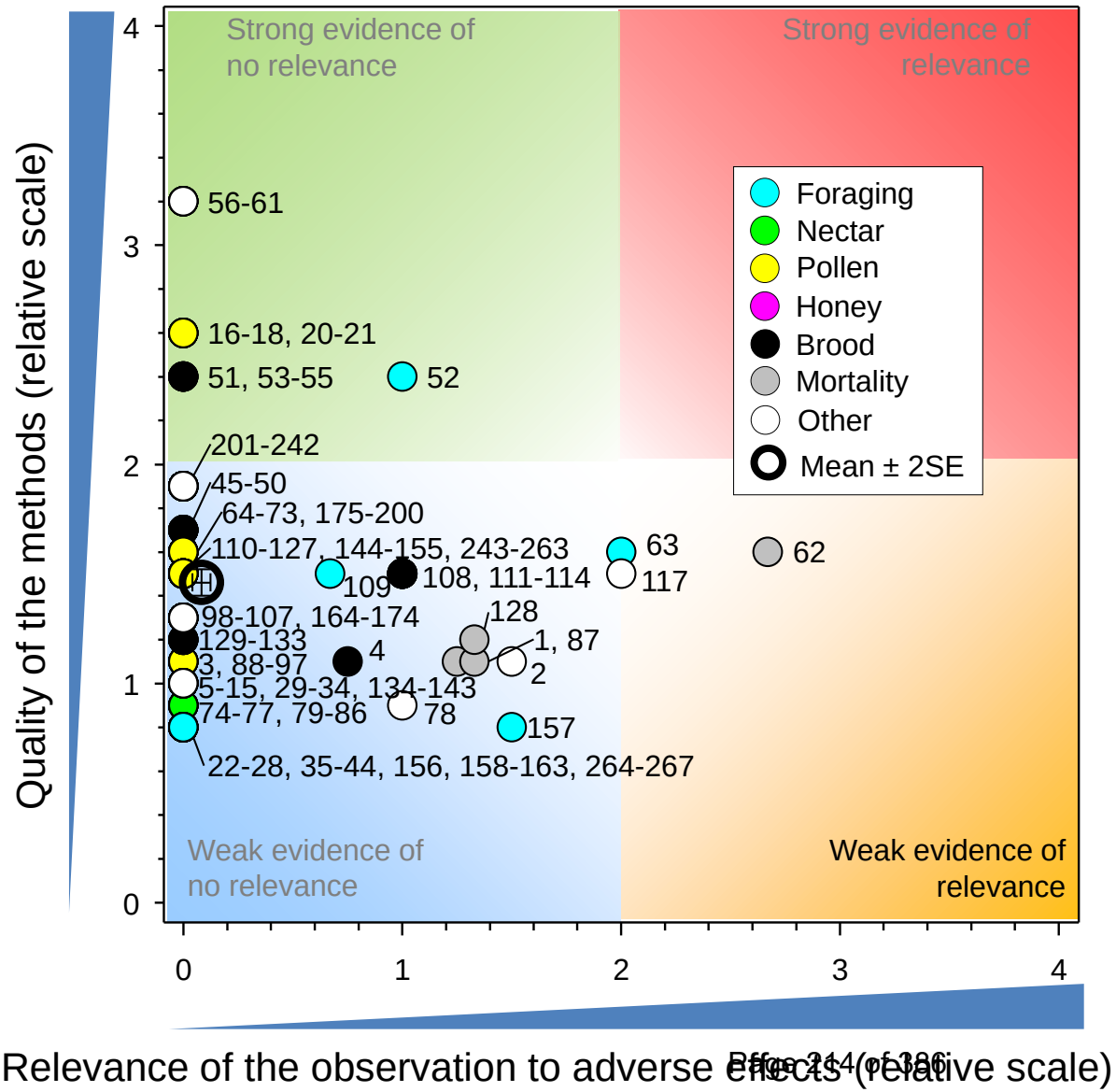
Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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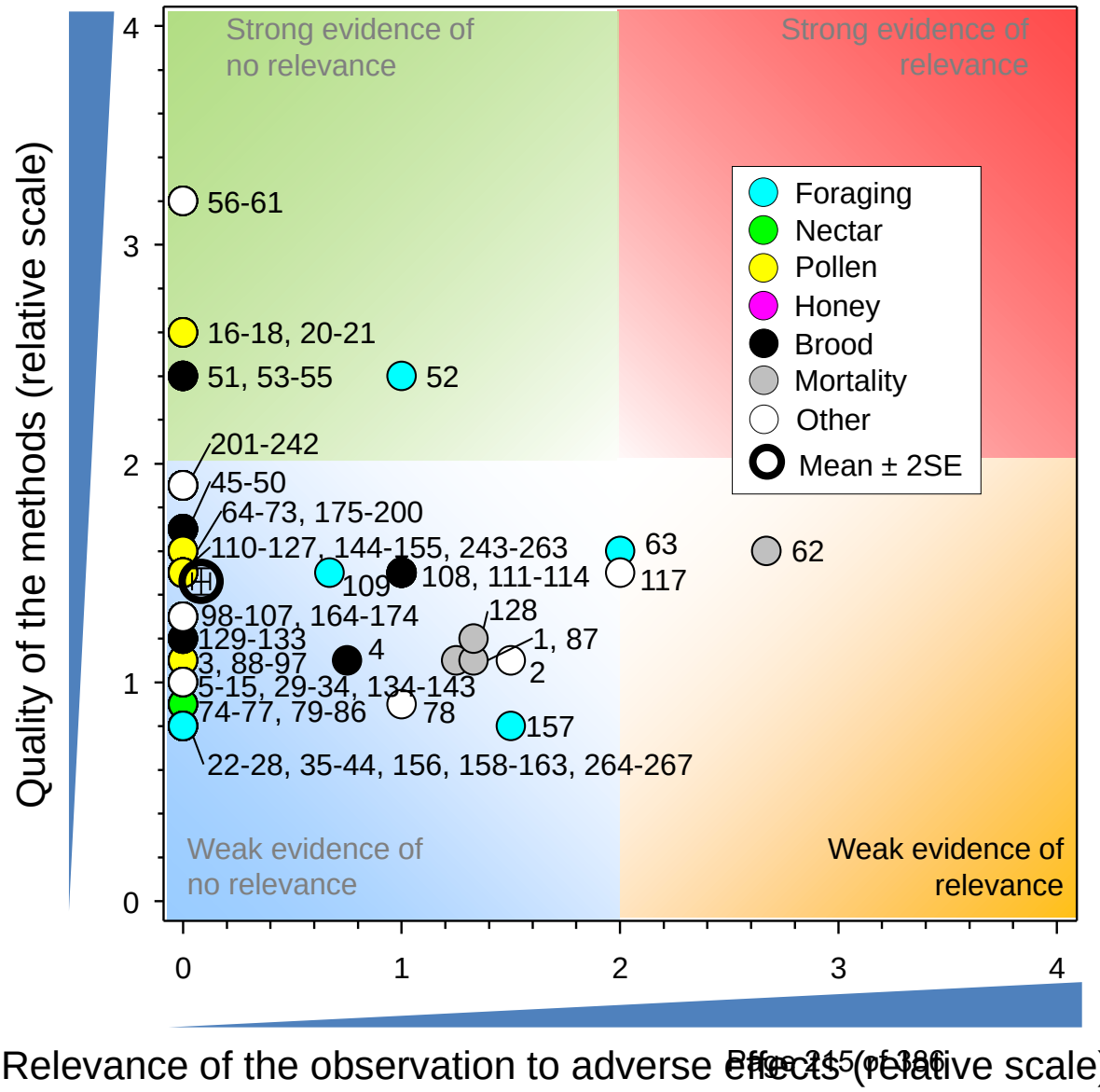
225 = (Syngenta 2010d) Resp 11

Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



226 = (Syngenta 2010d) Resp 12
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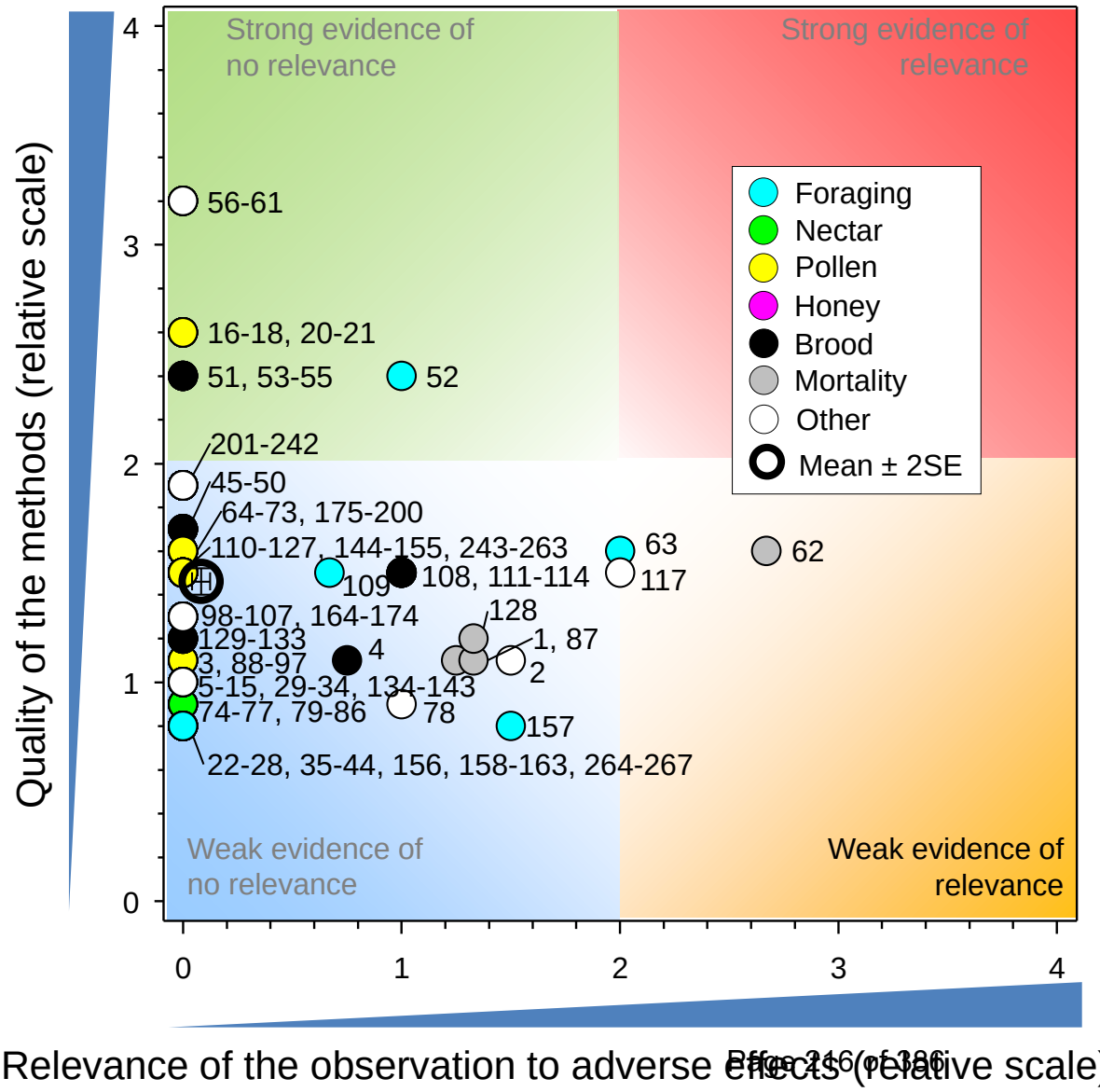
Effects of TMX on honeybees resulting from exposures via crops grown from treated seeds



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262 = (Syngenta 2010b) Resp 6
263 = (Syngenta 2010b) Resp 7
264 = (Thompson et al. 2016) Resp 1
265 = (Thompson et al. 2016) Resp 2
266 = (Thompson et al. 2016) Resp 3
267 = (Thompson et al. 2016) Resp 4

(Henry et al. 2015)
Paper: Henry M, Cerrutti N, Aupinel P, Decourtye A, Gayrard M, Odoux J-F, Pissard A, Rüger C, Bretagnolle V. 2015. Reconciling laboratory and field assessments of neonicotinoid toxicity to honeybees. Proceedings of the Royal Society B Biological Sciences 282:20152110

This study was designed to test hypotheses formulated to assess the disparity between laboratory feeding studies (acute and sublethal effects) and field investigations where the apical endpoints were colony metrics. The study tested the hypothesis that large-scale exposure to TMX residues in nectar resulted in increased mortality rate, precocious behavioural maturation, and decreased flight activity. Ultimately, there is an expectation of a decrease in colony Quality and ability to overwinter.

The focus of the WoE is on exposure of honeybees to TMX in plants that grew from dressed (Cruiser 280 g TMX/L) oilseed rape grown on a total of 288 ha (153 ha in 2013, 135 ha in 2014). The study was challenged by the occurrence of residues of imidacloprid in the nectar. The conclusion of the study was that a landscape scale in exposure does entail higher individual mortality of honeybees. Exposures in bee-relevant matrices are assessed in the corresponding WoE_{EXP}.

Responses 1-4: Quality of methods		**Score**
Experimental design and hypotheses	The objective of the study was to determine if an increase in landscape scale would influence the effects of TMX on honeybees. TMX-dressed winter oilseed rape (Cruiser) was sown in 2 consecutive years on 153 and 135 ha in 2013 and 2014, respectively, in the LTER Zone Atelier Plaine & Val de Sèvre areas of France. RFID technology was used to monitor the life histories of 6,847 individual bees in relation to levels of TMX. Although the initial study design included a desired gradient in TMX exposure concentrations across the fields, contamination of nectar with imidacloprid in the dietary nectar of foragers meant that exposure included a gradient to both TMX and imidacloprid concurrently. Cruiser® was applied with a TMX content of 280 g/L and the gradient achieved by placing honeybee colonies in different locations that varied with distance from source. 18 colonies bred from sister queens were set up in 10-frame Dadant hives and monitored in the field for colony dynamics and state of health. Hives were fitted with RFID data loggers to monitor the life history of a total of 46 cohorts of 100-250 honeybees during the oilseed rape flowering periods. The most exposed colony had to be excluded because it developed foulbrood syndrome concurrently with observed depopulation of the colony. Field exposure values ranged from 1 to 63 (mean ± SD = 15.7 ± 16.8) and exposure was calculated as the sum of all treated field areas with an ordinary inverse distance weighted interpolation (Figure 1). Variations associated with exposure were independent of total oilseed rape land cover and landscape complexity (Pearson's product-movement correlation, r = 0.32, p = 0.19 and r = -0.04, p = 0.86, respectively). The field exposure level was correlated to the neonicotinoid dietary residues of foraging bees using zero-inflated generalized linear mixed models (ZI-GLMM) because the residual data were neither normally distributed nor with equal variances.	**3**

	Colony dynamics included the systematic inspections for diseases as well as measurement of adult population size, honey stores, worker and drone brood production. Measurements were taken at the onset of flowering (18 April 2013 and 25 March 2014), and during the first and fourth week after the end of flowering. Mean weekly changes of colony parameters were computed for the five-week period referred to as *during* flowering and the three-week period referred to as *after* flowering. Colony changes were analysed against field exposure level using linear models (LM). Initial colony state was independent of the field exposure level (Pearson's product moment correlations, population size: r = -0.15, p = 0.53; honey reserves: r = -0.41, p = 0.090; total brood surface: r = 0.21, p = 0.40; worker brood surface: r = 0.22, p = 0.37; drone brood: r = -0.080, p = 0.742). Methods for the RFID were either cited or described in detail. The predictions of increased mortality, precocious behavioural maturation and decreased flight activity were assessed using appropriate and well described statistical procedures. Multi-residue analysis of samples collected from both flower nectar and honeybee dietary nectar were completed by ANSES, Sophia-Antipolis, FR. Because of the extent of the imidacloprid contamination, samples were also collected from non-experimental oilseed rape fields within the 450 km^2 study area to expand the data base. A total of 73 oilseed rape fields were thus sampled for nectar between 15 and 24 April 2014. Residues were quantified (limit of detection = 0.1 ppb, limit of quantification = 0.3 ppb) by liquid chromatography with electrospray tandem mass spectrometry[25]. The exposure concentrations were unclear and expressed as exposure units (***major weakness***) defined as "one field exposure unit is virtually equivalent to 1 ha of treated oilseed rape within a 1 km distance from the colony, or e.g., 4 ha at a 2-km distance". Statistical methods were poorly described but the results were presented in an acceptable manner.	
Use of GLP and QA/QC.	Non-GLP but methods were well established, cited or briefly described. QA and QC procedures were not reported.	**2**
Exposure concentrations	RFID data were collected from three cohorts and a total of 6,847 individual honeybees and data for 17 honeybee colonies; the exposures were expressed as exposure units and ranged from 1 to 63 units (Figure S2A). Thiamethoxam concentrations ranged from 0.1 to 0.8 ug/kg. Residues remained undetected in dietary nectar in colonies with limited field exposure level (< 8 units) and were only found at highest exposure levels (8 to 63), validating the experimental gradient of field exposure to thiamethoxam (ZI-GLMM, n = 51 [3 samples × 17 colonies], z = 2.91, P = 0.003). The model intercept is not significantly different from zero (z = 0.37, P = 0.71), further confirming that the least exposed locations may be viewed as thiamethoxam-free environments for a sound basis of comparison. imidacloprid concentrations ranged from 0.1 to 1.0 µg/kg in 13 out of 17 colonies (p 4) and correlated with the TMX concentrations (Figures S2B and C). imidacloprid contamination forced the authors to use a combined approach. Concomitancy of thiamethoxam and	**1**

[25] Martel A-C, Mangoni P, Gastaldi-Thiery C. 2013. Determination of neonicotinoid residues in nectar by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Euro Reference J. 11, 18–21.

	imidacloprid residues in dietary nectar samples (z = 6.93, P < 0.001) is depicted in Figure S2C and compromises interpretation of effects because attribution cannot be to TMX alone.	
Transparency of data.	Some raw data were included in the supplementary information (SI 2-4); the majority was presented in summary form.	**2**
Number of samples and replication.	Sample sizes were adequate although it was unclear if the results for the two years were treated as independent replicates. A power analyses was conducted (Figure 3) and demonstrated that a sample size 17 was adequate for survival (mortality) metrics.	**3**
Overall evaluation of methods	Computed mean of above	**2.20**
Score for expert judgment on quality of the study- the exposure concentrations were unclear and expressed as exposure units (major limitation)	**0.5**	**1.10**

Response 1. Effects on honeybee mortality rates		**Score**
Statistical significance of responses	Honeybees disappeared at a faster rate with increasing field Exposure-units and this excess mortality increased over time (SI, Table S1). Baseline mortality increased by 10.1% (CI95% = 3.0–17.7%) per 15 field exposure units (Cox PH survival analysis, n = 78,716 daily records for 6,847 bees, z = 2.85, p = 0.004). However, a highly significant deviation from hazard proportionality (x^2 = 258, p = 0.001) was detected indicating that the excess mortality was not stationary but increased with time. The field exposure effect was reassessed and expressed as an interaction with time and a better fit was achieved (Cox PH, field exposure effect: z = 3.52, p = 0.001). Excess mortality was raised by 5.6% per 15 field exposure units per additional week, i.e. from an average 5.6% excess mortality at the onset of flowering to 22.4% after three more weeks had passed. This time-mediated survival pattern was consistent between the two study years (Cox PH, inter-annual variations: z = 0.41, p = 0.68), and might be interpreted either because of the accumulation of neonicotinoid residues in food and hive materials over time, with a delayed effect, or as the emergence of a chronic exposure effect. The field exposure effect on honeybee mortality was not moderated by the environmental covariates related to landscape complexity or oilseed rape total land cover, or by their two-way interactions. Both models (model #1 and #2) indicated that "field exposure" was a significant explanatory variable (P = 004, P<0.001, P = 0.002) for all bees, just-emerged bees, and forager bees only, respectively, for model #1. The only significant explanatory variable for model #2 was "field exposure" (Cox PH survival analysis; n = 78,716 daily observations on 6,847 bees; z = 2.96; P = 0.003; Table S2).	**4**
Concentration- or dose-response	The exposure concentrations were unclear and expressed as exposure units; however, application of models to the data indicate that exposure concentration of TMX positively correlated with exposure unit. No r^2 or r values were presented.	**1**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Despite this established link between exposure to neonicotinoids and adult mortality, honeybee colonies could compensate and maintain the apical endpoints of honey production and population size.	**0**
Mechanism and or mode of action of effect explained	Exposure to imidacloprid and TMX concurrently was associated with a significant increase in mortality of free-ranging honeybees. Despite this established link, colonies could compensate for the increase in	**0**

	mortality and maintain the apical endpoints of honey production and population size by delaying drone brood production and increasing worker production. Further, analyses confirmed that field exposure accelerated the disappearance of both forager and just-emerged bee cohorts (Figure 2 and Figure 3a and 3b). The "effect" could not be attributed to TMX alone because of the concomitant presence of imidacloprid.	
Overall evaluation of relevance (computed)		**1.25**
Overall evaluation of relevance (SEJ). There was no persistent adverse effect to apical endpoints of honey production or population.		**0**

Response 2. Effects on honeybee precocious behavioural maturation		**Score**
Statistical significance of responses	There was no evidence that age at first exit from the hive was adversely affected; however, there was a significant non-stationarity, i.e. a significant variation over time, in the rate at which just emerged monitored bees performed their first flights in relation to field exposure (Model 1 in SI, Table S3). Up to the 10th day of monitoring, first flights occurred 19.6% earlier for an average field exposure of 15 units. But up to the 20th day of monitoring, first flights occurred on average 8.8% later in the honeybee life for an average field exposure of 15 units. This offset the apparent first flight precocity on age at first exit (SI, Table S3). All P values were > 0.05 with one exception - field exposure with deviation from temporal stationarity.	**4**
Concentration- or dose-response	The exposure concentrations were unclear and expressed as exposure units; however, application of models to the data indicate that exposure concentration of TMX positively correlated with exposure unit; however, field exposure was not a significant effect	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	This non-stationarity of age at first flight along the field exposure gradient suggests that a portion of the monitored young bees indeed became precocious foragers while the others were compelled to spend a longer lifetime as in-hive worker to cope with the increased nursing tasks.	**2**
Mechanism and or mode of action of effect explained	In spite of the excess mortality and precocity measured at the individual scale, highly exposed colonies did not show altered performance per se in terms of population growth and honey and brood production.	**0**
Overall evaluation of relevance (computed)		**1.50**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee flight activity		**Score**
Statistical significance of responses	There was no significant adverse effect on daily rate of flight activity (SI, Table S4).	**0**
Concentration- or dose-response	The exposure concentrations were unclear and expressed as exposure units; however, application of GLMM models to the data (number of log-transformed number of detection events per day and per individual) indicate that exposure to TMX had no effect on flight activity ($p = 0.17$, $p = 0.79$; Table S4).	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**

Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee colony dynamics.		**Score**
Statistical significance of responses	There was a change in the way reproductive effort was allocated between female (worker) brood and drone (male disperser) brood. The relative proportions of worker brood versus drone brood production (SI, Figure S3) changed. During flowering, the most exposed colonies tended to invest more in worker brood production at the expense of drone brood production (SI, Figure S3A). Drone brood development was delayed in exposed colonies; after flowering, drone brood production followed the field exposure gradient, being significantly higher in the more exposed hives (SI, Figure S3B). Field exposure was not considered to be a significant explanatory variable for population size, honey reserves, total brood area, worker (female) area, drone (male) area during flowering (Table S5). Field exposure was a significant explanatory variable for drone brood area after flowering, only.	**3**
Concentration- or dose-response	The exposure concentrations were unclear and, apparently, the gradient of concentrations was presented in the supplementary tables and figures.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The authors postulate that drones are more energetically costly to the hive than workers because they do not forage and speculate that delayed drone production could disrupt biological synchrony. There was no evidence of this in the apical endpoints measured in this study.	**0**
Mechanism and or mode of action of effect explained	Colonies compensated to preserve population size and honey production. The most exposed colonies modified the timing of their reproductive investment, delaying drone brood production in favor of increased worker brood production.	**0**
Overall evaluation of relevance (computed)		**0.75**
Overall evaluation of relevance (SEJ).		

Narrative

Explanations on the disparity of results between laboratory and field studies have been postulated and include the following:

1. Laboratory exposures use higher effect concentrations that are unrealistic
2. Laboratory studies generally use methods that measure acute effects rather than chronic effects
3. Field studies inherently incorporate compensatory influence of demographic regulation mechanisms and honey storage (aka resilience).
4. Laboratory exposure studies do not take into consideration the time lag effect that might occur such as colony overwintering weakness or increased susceptibility to disease Spatial scales might influence the ability to detect an adverse effect; e.g., foraging range scales for field studies generally use in-crop exposure and will not elucidate homing failure of honeybees

Despite an apparent link between neonicotinoid exposure and increased mortality of individual free-ranging foragers, colonies appeared to be able to compensate for the excess mortality so as to preserve unaltered performance in terms of population size and honey production. Instead, the most exposed colonies modified the timing of their reproductive investment,

delaying drone brood production in favour of increased worker brood production. Risk assessors must consider the scientific evidence for behavioural disorders triggered by trace levels of neonicotinoids.

Expert Judgement		
QA	Yes	May 31, 2016
SEJ	Yes	May 31, 2016

(Pilling et al. 2013)
Paper: Pilling E, Campbell P, Coulson M, Ruddle N, Tornier I. 2013. A four-year field program investigating long-term effects of repeated exposure of honey bee colonies to flowering crops treated with thiamethoxam. PLoS ONE 8:e77193.

This is a summary of a four-year study of the long-term effects of repeated exposure of honey bee colonies to flowering crops treated with thiamethoxam (TMX). The major weakness to this paper was the exposure analyses and the statistical analyses of the data. The reliance on best professional judgement for interpretation of results could be construed as a weakness because of the uncertainty such an approach introduces. The objectives were to quantify the level of honey bee exposure to residues of TMX and clothianidin (metabolite) in pollen and nectar collected by bees from maize and oilseed rape grown from treated seed and to determine residues in colony products (bee bread stored in cells, nectar, honey, wax and royal jelly). This aspect is covered by the WoE_{EXP}. The second objective was to investigate if exposure to such residues in pollen and nectar from field treated maize and oilseed rape adversely affected colony Quality and survival following repeated single treatment crop exposure each year over a four-year period. The field study maximized the potential exposure of bees by restricting the honey bees to tunnels built over the TMX-treated crop to ensure exposure to crop-related TMX and tried to minimize confounding effects attributable to other pesticide applications. Criticisms were levied by Hoppe et al.[26] and effectively rebutted by Campbell et al.[27].

Responses 1-11: Quality of methods		**Score**
Experimental design and hypotheses	The study with maize involved three sites (Alsace, Lorraine, and Aveyron), where treated seeds (flowable mixture at 420 g/L) were planted (var. not provided), and was conducted between 2006 and 2010. The study with oilseed rape involved two sites (Alsace and Picardie) which were planted with var. Roxet (p 3) treated with TMX (280 g/L) was conducted between 2005 and 2009 (Table 2). Average field size was 2 ha (p 8). Fungicides were also used (metalaxyl-M at 1.33 g/L and fludioxinil at 3.33 g/L) on the maize and on the oilseed rape (metalaxyl at 33.3 g/L and fludioxinil at 8.0 g/L). The application rates for maize were the nominal label rates of 88.2 g a.s./ha (0.85 mg a.s./seed); for oilseed rape the rates were 12.6 g a.s./ha (0.02 mg a.s./seed). The spring barley rate was 77 g a.s./ha or 0.03 mg a.s./seed which superseded the planting of oilseed rape (p. 3). Honey bees were exposed to the crop inside 3 tunnels (40 x 5 m) covering the treated crop and one tunnel on the adjacent control at the start of flowering BBCH 63 for maize and BBCH 60-62 for oilseed rape. There was one colony per tunnel comprising ~10 to 20K bees in two boxes with 10 combs each. The exposure periods were between 4 and 10 days for maize and between 9 and 14 days for oilseed rape (p 4). Plants were collected on days 1, 7, and 9 after exposure of the hives in the TMX treatments and on day 1 of the control. Forager bees were collected on days 1, 7, and 9 during flowering at the hive entrance which was sealed and immediately frozen. The bees were processed at the LAVES bee institute to obtain pollen and stomach nectar. Bee bread stored in hive cells, nectar and wax	**2**

[26] Hoppe PP, Safer A, Amaral-Rogers V, Bonmatin J-M, Goulson D, Menzel R, Baer B. 2015. Effects of a neonicotinoid pesticide on honey bee colonies: A response to the field study by Pilling et al. (2013). *Env Sci Eur* 27

[27] Campbell P, Coulson M, Ruddle N, Tornier I, Pilling E. 2015. Authors' response on Hoppe et al. (2015) "Effects of a neonicotinoid pesticide on honey bee colonies: a response to the field study by Pilling et al. (2013)". *Env Sci Eur* (2015) 27–28. *Env Sci Eur* 27:

	samples from combs were collected once on the day hives we set up and at 1, 7, 9 and 20 days after the exposure of the bees to the crop and thereafter monthly until the end of September. When possible honey from the combs was also collected on the same days. The extraction methods differed depending on the medium and were described but not in detail (minor weakness). The method of analyses was high performance liquid chromatography reported to be LC-MS/MS spectrometry. Some QA details were reported for analytical data. For the multiple exposure study comprising 3 long-term overwintering trials with maize in Lorraine, Alsace and Aveyron regions of France started in 2006 and the two trials with oilseed rape in the Picardie and Alsace regions of France started in 2005. At each site, there was one control field and one treated field separated by ~2 km. Each field was ~2 ha. The application rates for maize were the nominal label rates of 88.2 g a.s./ha (0.85 mg a.s./seed); for oilseed rape the rates were 12.6 g a.s./ha (0.02 mg a.s./seed). The spring barley rate was 77 g a.s./ha or 0.03 mg a.s./seed which superseded the planting of oilseed rape (p. 3). There was one colony established in each field in two brood bodies comprising 5-8 brood combs and 15-20 food combs. Colonies were relocated after flowering to woodland areas relatively free of pesticides in the Alsace region for the northern sites and Midi-Pyrénéés for the southern trial. Control colonies were kept apart from the treated colonies to avoid cross contamination. Colonies were monitored throughout the year and before and after overwintering; hive weights (Figure 11), Quality of the colony (# adult worker bees); presence of healthy queen and day-old eggs; pollen and nectar storage area; brood development (area with eggs, larvae and capped cells) were assessed. To prevent swarming, the colonies were split in late spring in subsequent years (i.e., 2006 and 2007 for the oilseed rape and 2007 and 2008 for the maize). In the final year of the study swarming was prevented by removing some brood and store combs and replacing them with empty combs (p 10). Brood assessments were conducted in March and April to assess overwintering. Detailed assessments were also completed before and after the exposure periods and every 10 days once relocated to the monitoring sites. Residues were measured in nectar and pollen from plants in the treatment fields as well as plant tissues themselves. Residues were measured in nectar and pollen collected by bees by extracting these substances from forager bees (n = 50 pooled). Results were presented as mean values of 6 hives for each site. Statistical analyses were incomplete because the replicate units were the fields (n = 3 for maize and n = 2 for oilseed rape); therefore, best professional judgement was relied upon for the interpretation of effects (**major weakness).** Agronomic crop differences precluded combining the maize and oilseed rape data. Only the biological data for oilseed rape at the site in the Alsace region were included in the paper as an example of typical data obtained in this study. This site was chosen because it had the highest reported residues of TMX and clothianidin in nectar (minor weakness). The effect observations were representative of those for the other oilseed rape and maize sites in the other regions.	
Use of GLP and QA/QC.	There was no mention of GLP in this study; however, analytical QA was included. LOQs were 0.5 and 1 µg/kg for TMX and clothianidin, respectively, for nectar and honey and 1 µg/kg for both TMX and clothianidin for bee pollen, bee bread and whole plant tissues. Residues were presented in box whisker plots skewed because of non-detects.	**2**

Exposure concentrations	The concentrations added to the seeds and the rate of application were the same for each site within each crop species (e.g., single application rate for maize and for oilseed rape). There was no exposure concentration gradient.	**2**
Transparency of data.	Only summary data were presented in this paper; however, the original study reports probably contain the raw data; SIs contained additional information.	**2**
Number of samples and replication.	There were 2 independent crop species with 3 and 2 independent field replicates; there was one control field for each field site (n = 6). Within a replicate there were multiple measures over time and the sample size differs depending on the endpoint metric and method of measurement. The study was repeated each year for a total of 3 years.	**2**
Overall evaluation of methods		**2.00**
Statistical analyses were not conducted and no P values were reported which constitutes a **major weakness.**	**0.5**	**1.00**

Response 1. Effects on number of bees in front of the hive (dead bee traps and linens)		**Score**
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. Mean number of dead bees per hive per day were plotted for the control and TMX oilseed rape treatment for years 2005, 2006, 2007 and 2008 (Figure 6). Figures S1-S4 contained the data for the other sites. The number of dead bees was low in both the control and TMX treated fields (below 100 bees) with one exception (Aveyron 230 bee in the control) and mortality was greater at the beginning of the exposure period than at the end.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee foraging activity in TMX-treated oilseed rape		**Score**
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. Foraging activity for the control and TMX oilseed rape treatment was summarized for years 2005, 2006, 2007 and 2008 (Figure 7). Figures S5-S8 contained the data for the other sites. Over the four years the foraging activity of bees were similar between the control and TMX-treated oilseed rape crop and likewise for the other sites with both rape and maize. Flight intensity decreased toward the end of flowering in both the control and the TMX fields.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**

Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee pollen loads in TMX-treated oilseed rape		**Score**
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. Pollen loads collected by honeybees at the hive entrance from foragers showed the mean proportion of oilseed rape pollen on individual sampling days varied from 15-64% in the TMX treatment and 7-75% in the control over the 4-y study period. For maize, the proportion varied from 0-82% in TMX treatment and 0-55% in the control over the 4-y study period.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on colony Quality of TMX-treated oilseed rape – number of bees		**Score**
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. Mean number of dead bees per hive were plotted for the control and TMX oilseed rape treatment for years 2005, 2006, 2007 and 2008 (Figure 8). Figures S9-S12 contained the data for the other sites. The fluctuations in number of bees per colony were very similar in both treatments. Colonies increased in the spring as the food supply increased in both the exposure and in the monitoring sites. Upon hive separation at the end of the exposure period, colony size decreased in both treatments. Upon production of a fertile queen, colony size increased in both treatments through June and July and then declined in the fall as egg-laying stopped.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**

Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-9. Effects on colony Quality of TMX-treated oilseed rape – comb area with brood (eggs, larvae and pupae) and food (nectar and pollen)		**Score**
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. Mean comb area with brood and food for the TMX and control are summarized in Figures 9 and 10, respectively. The comb areas with brood and food for the other sites are summarized in Figures S13-20. The patterns for brood and food development were similar between the control and TMX treatments for all sites and both crop species. Brood development increased up to the last assessment at which time is a decrease due to lower food and a seasonal decrease in egg laying (p12). Brood areas increased in the subsequent spring as food became available and egg laying commenced. The natural cycle of brood development was observed in colonies at all sites.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on colony Quality of TMX-treated oilseed rape –healthy queen and day-old eggs		**Score**
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. During the study, some colonies produced male brood only, indicating the absence of a healthy egg-laying queen. Mean loss of colonies ranged from 0 to 2.7 colonies per year across all five sites (total of 60 colonies), with similar losses between treated and control sites (Table 2). The frequency of queen replacement and colony loss was within what is expected in normal beekeeping practice.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 11. Effects on colony Quality – colony weight		Score
Statistical significance of responses	There were no statistical analyses of these data and no P values reported. Mean colony weights for both treatments are presented in Figure 11; those for the other trial sites in Figures S21-24. Generally, the patterns for weight gain and loss were similar at all sites and for both crop species. Changes could be attributed to normal bee-keeping practices.	**0**
Concentration- or dose-response	There were no significant effects and a concentration-response was not applicable.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

Residues for each site measured in plant tissue and bee and hive pollen for the tunnel study with TMX-treated maize in the first year (Fig. 2) and over two years in a rotation study with TMX-treated maize (Fig. 3) were provided as box whisker plots. Residues for each site measured in plant tissue and bee and hive pollen for the tunnel study with TMX-treated oilseed rape from year 1 (Fig. 4) and from oilseed rape following barley rotation (Fig. 5) were provided as box whisker plots. Summary data for all trials is in Table SI. These data are fully discussed in the WoE_{EXP}. Exposure residues for the field study with bees generally followed similar trends. The range of values (p. 11) for TMX and clothianidin in plant tissues for maize and oilseed rape were from <1 to 8.5 µg/kg and from <1 to 5.5 µg/kg, respectively; the corresponding range of values in pollen collected by bees in all maize sites was from <1 to 2 µg/kg. Conclusion was that residues of both TMX and its metabolite clothianidin were typically low in pollen and nectar.

Conclusion was that residues in honey and pollen of TMX and clothianidin when applied at realistic field-rates do not result in adverse effects to honeybees. There was only one site with control and treated plots and no replication; only one hive was placed into the treated plot; therefore, a concentration-exposure response was not applicable (NA). That said, the trials were repeated each year for either three or four years.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 2, 2016

(Pohorecka et al. 2012)
Paper: Pohorecka K, Skubida P, Miszczak A, Semkiw P, Sikorski P, Zagibajło K, Teper D, Kołtowski Z, Skubida M, Zdańska D, Bober A. 2012. Residues of neonicotinoid insecticides in bee collected plant materials from oilseed rape crops and their effect on bee colonies. Journal of Apicultural Science 56:115-134.

The aim of the study was to measure the concentration of several neonicotinoid insecticides (including TMX) in nectar, pollen, honey, bee bread and to assess the potential short- and long-term effects on honeybee colonies. This WoE is focused only on TMX effects whereas the exposure WoE is provided elsewhere. Other neonicotinoids were used as foliar sprays and are not included in the characterization of exposure.

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in Poland at an unreported location. In 2010, two winter oilseed rape fields (wOSR) (field A - 41 ha - and field - B 35 ha) were treated with TMX (CRUISER OSR 322 FS) and imidacloprid CHINOOK PLUS 500 FS) as seed dressing, respectively. In 2012, three separate spring OSR fields (field C - 29 ha, field D - 21 ha and field E - 17 ha) were planted with OSR seed treated with TMX (CRUISER OSR 322 FS), clothianidin (MODESTO 480 FS), and imidacloprid (CHINOOK PLUS 500 FS), respectively. Therefore, only the TMX data from Fields A and C for the years 2010 and 2012, respectively, were assessed in this WoE. Distances between the fields were not reported (*weakness*). All the crops were also treated with herbicides, fungicides and insecticides from other chemical classes as required by good agricultural practice. The detailed description of the products used was provided (Table 1). The blooming period of wOSR was 31 Apr to 21 May 2010. The blooming period of sOSR was from the 14 Jun to 2 Jul 2012. Seed was not analyzed for amount of a.s. and the rate of treatment was not reported (*weakness*). Hives were placed into fields on April 30, 2010 until July 21, 2010. The hives used in this study were assessed for health and disease status prior to use in the study. Ten colonies of honeybees (*Apis mellifera carnica, Apis mellifera caucasica*) with ~equal colony Qualitys and similar populations were placed near each oilseed rape field, throughout the flowering period (ca. 3 weeks from April 30 to 21 May 2010 and from June 14 to July 2, 2012). In each group, an additional five hives equipped with pollen traps were designated only for collection of pollen loads. Two control groups of hives (one in 2010 and one in 2012) were in an area where no rape was grown. The hives in 2012 were transported from the field to a stationary apiary on July 30, 2012. Monitoring continued until the end of the season for each year. The population size was measured at set up and every three weeks thereafter until the end of the season and included determinations of colony development and health reflected, in part, by the number of combs covered by bees and the brood area, worker biomass, infections and infestations (diseases and pests), and bee mortality in the hive and at the entrance to the hive (hive bottom boards and white trays on ground in front of hive entrances). Honey yield per colony was	**3**

	determined by weighing the harvested honey. In September, hives were prepared for winter by feeding the honeybees and treating for mites. During flowering of rape, samples of nectar were collected from rape flowers protected from insects by 16 m^2 mesh tunnels. A minimum of six samples were collected from each field during the flowering period. Nectar flow from combs (100 g) was taken 7 and 14 d after the colonies were placed on the fields. Honey (100 g) was harvested separately for each colony (from honey chambers only) once, about one week after the blooming period. During the 3-week period of blooming, all of the pollen loads that the bees had collected within a 3 to 4-day period were taken separately from the pollen traps of each of the five colonies. Samples of bee bread (app. 10×10 cm pieces of combs) were taken once, after the blooming period. About 100 of bee workers were taken from brood chamber one time, after the oilseed rape blooming period. Samples of nectar, honey, and pollen were taken for identification of source. Bees were also collected for residue analysis but were not included in this WoE. All collected samples were frozen and stored at a low temperature of about -20°C. Honey yield was measured (see above). The residue analysis was described in detail and is addressed in an accompanying WoE on exposure. No residues of any seed treatments were detected in nectar, honey or pollen from the controls of wOSR (Table 6). TMX was detected in 65 % of all (n = 212) nectar and honey samples collected and in 37% of all (n = 205) pollen and bee bread samples collected (Table 5). Statistical analyses were carried out using Statistica 8 software and involved means comparisons (Student's t-test, ANOVA procedures followed by Tukey test for parametric procedures; non-parametric procedures included Mann -Whitney U-test or Kruskal-Wallis test). Means and medians were calculated but other centiles were not (*potential weakness*). Spearman's rank correlation was used to assess relationships between variables. Proportion of pollen from *Brassica napus* in the pollen collected by bees during flowering of rape in the fall and spring was large in 2010 and 2012, 92.3 and 98.0%, respectively (Table 3).	
Use of GLP and QA/QC.	Non-GLP only because there is no statement saying GLP was followed. From the description of the materials and methods, the spirit of GLP was followed as purities were stated, source of chemicals identified, and procedures described in detail, blanks were used and calibration described, recovery efficiencies for all matrices were stated, LODs and LOQs provided, use of standards.	**2**
Exposure concentrations	One treatment field and one control field for each year. Concentrations were measured in a variety of matrices to assess exposures.	**4**
Transparency of data.	Summarized and raw data presented in tables. Some raw data available supplementary.	**2**
Number of samples and replication.	Multiple measurements taken over time for each of 2010 and 2012 but only one treatment and one control, each with 10 or 5 hives (pseudo-replication).	**2**
Overall evaluation of methods	Computed mean of above	**2.60**
Score for expert judgment on quality of the study	**1**	**2.60**

Response 1. Effects on adult bee mortality		Score
Statistical significance of responses	No bees were found dead during the exposure period of April 30 to July 21, 2010. Mortality averaged 18 and 4 bees per colony in the TMX exposed group in 2010 and 2012, respectively. Mortality was low while hives were in the field and after transport to the stationary apiary (see Section 1.2.1). There was no treatment effect in either year (p = 0.961).	**0**
Concentration- or dose-response	There was only one field for each treatment in both years: control and TMX; therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on colony health – infectious diseases and parasites		Score
Statistical significance of responses	The treatments (control and TMX) neither differed significantly in 2010 (Kruskal-Wallis test, H = 0.461, p = 0.793) nor in 2012 (Kruskal-Wallis test, H = 6.35, p = 0.095) with respect to *Nosema* spp.; and, clinical symptoms of any diseases were absent in all treatments (Section 1.2.1). No viruses except a few with DWV were found. *Varroa* infestations were low.	**0**
Concentration- or dose-response	There was only one field for each treatment in both years: control and TMX; therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3-4. Effects of TMX on colony Quality –population size and brood areas		Score
Statistical significance of responses	Population size measured by both the number of combs covered by bees and the brood area was not significantly different from that in the control group in either year. There were no significant differences between treatments (P >0.05) in terms of the number of dead bees reported while colonies were developing and waning (Tables 9 and 10, Group A and C, respectively). All colonies developed normally and there were no significant differences (P >0.05) between treatments.	**0**
Concentration- or dose-response	There was only one field for each treatment in both years: control and TMX; therefore, a concentration-exposure response was not applicable (NA)	**NA**

Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-6. Effects of TMX on colony honey production and pollen harvest from combs by bees		**Score**
Statistical significance of responses	Honeybees collected more nectar and pollen from spring rape than from winter oilseed rape (p. 126). In 2012, the honey yield for the TMX-treated field was 14.3 kg/colony and similar to those for the controls (p = 0.106). Similarly, the treatments were similar for pollen harvest.	**0**
Concentration- or dose-response	There was only one field for each treatment in both years: control and TMX; therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no significant response was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no significant response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

There were no adverse effects of TMX on honeybee mortality, brood development, colony Quality or health, or honey yield despite TMX residues measured in nectar from plants, nectar from combs, honey, pollen and bee bread. No matrices (bee bread, nectar collected by bees, nectar from plants, hive honey, or pollen) had measured TMX residues above the chronic NOAED of 10.6 ng/bee/d for honey bees (see WoE_{EXP}).

Expert judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 2, 2016

(Syngenta 1998b)
Report: Syngenta. 1998. Semi-Field Test: Effects of Oil-Seed Winter-Rape Grown from Seeds Dressed with A9700 B on the Honey Bee (*Apis mellifera* L.). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_0822 - A9700B. 27 p

The semi-field study involved one site divided into 2 plots on which TMX-treated OSR and un-treated OSR were grown. Cages were established in triplicate on each plot and one hive was placed into each cage. The objective was to determine the effects of TMX on honeybees.

Responses 1-7: Quality of methods		**Score**
Experimental design and hypotheses	Honeybees in cages (semi-field) were placed into plots near Pforzheim, Germany with oilseed rape (var. Evita) planted with either TMX-treated seed (TMX treatment) or un-treated seed (control treatment) that were ~3.6 m by 2.4 m. Sowing rates in both treatments were 14.5 kg/ha and were done with a pneumatic seeder. Cages were established on the plots before flowering. Hives of similar Quality, comprising 3 combs and queens from one breeding line, were introduced to the cages in the evening of August 3, 1998 when the OSR was at full flowering. The front of the hive was equipped with a dead bee trap (DBT). There were three cages for each treatment with one colony in each cage. Meteorological data were reported (Table 6; Appendix A1). The measurement endpoints included honeybee mortality at the edge of the crop and in the DBTs starting the day after the hives were placed into the cages and every day for 7 d. Flight intensity was observed and recorded in the morning after the hives were placed into the cages and 3 times a day for 5 min. each on August 4-6 and once a day from August 7-11, 1998. The number of foraging bees flying over the crop in an area of 1 m^2 were counted. Flower visits were also recorded to determine if TMX served as a repellent for honeybees (Table 4). The condition of the colonies and development of bee brood was assessed on three occasions – one day before, 9 and 28 d after exposure. This entailed measuring the Quality of colony as the number of combs covered with bees; the presence of healthy queens (eggs and queen cells); pollen and nectar storage area; and, the comb area containing brood (eggs, larvae and capped brood). Observations of bee behaviour were also reported. The influence of TMX was evaluated by comparing the results for the TMX treatment with those of the control treatment. No statistical procedures were applied to the data (**major weakness**).	**2**
Use of GLP and QA/QC.	GLP compliant with signatures, QA statement; the study plan was provided with deviations and amendments.	**3**
Exposure concentrations	No TMX or clothianidin residues were measured in any matrices. Seeding rates were not verified. There is no actual measure of exposure.	**0**
Transparency of data.	Raw and summary biological data were reported (except for behaviour); no analytical chemistry was included.	**2**
Number of samples and replication.	One field, two plots (TMX and control) each with 3 cages and one hive per cage. No replication just pseudo-replication.	**1**
Overall evaluation of methods		**1.60**

Score for expert judgment on quality of the study–no statistical analyses of data comprise **major weaknesses**	**0.5**	**0.80**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values reports. There were no adverse effects of TMX on honeybee mortality (Figure 1; Tables 7 and 8, Appendix A2). Mortality was either similar to or lower than that in the control treatment. Daily mortalities ranged in the TMX treatment between 4 and 24 dead bees/hive/day compared to that in the control which ranged between 6.3 and 30.3 dead bees/hive/day.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effects were apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effects were apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on flight intensity – number of bees & time spent on flowers		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values reports. Flight intensity was similar between treatments (Figure 2; Tables 9-10, Appendix A2) with mean flight intensities for the duration of the observation period of 7.3 and 8.1 bee/m^2 for the TMX and control treatments, respectively. Similarly, the duration of flower visits was similar between treatments.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effects were apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effects were apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-6. Effects on colony development –brood development (comb area with eggs, larvae and capped brood cells)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values reports. The comb area with eggs, larvae and capped brood cells all decreased in the hives over the observational period in both treatments which was expected from caging the bees for 8 days and limiting food supply (Tables 11 and 12, Appendix A2). The queens survived in good condition and eggs were present.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**

Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effects were apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effects were apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7. Effects on honeybee behaviour		**Score**
Statistical significance of responses	There were no reports or observations of abnormal behavior in either the TMX or control treatments (subsection 6.5, p. 17). No data were presented.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effects were apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effects were apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 2, 2016

(Syngenta 1998a)
Report: Syngenta. 1998. Tunnel Test: Effects of Sunflowers Grown from Seeds Dressed with A-9567B on Honey Bees (*Apis mellifera*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_0957 - A9567B. 40 p

A semi-field (tunnels) study was conducted in Merainville, central France (Beauce area) to evaluate the effects of TMX-treated sunflower seeds on mortality, behaviour and foraging activity of *Apis mellifera mellifera*. Exposure of honeybees to residues in bee matrices is evaluated in the WoE_{EXP} based on Report CGA293343_1363-A9567B[28].

Responses 1-6: Quality of methods		Score
Experimental design and hypotheses	Sunflower seed (var. Cadasol) was treated with TMX (A-9567B) at two loading rates (350 g and 700 g a.s./100 kg seed). A reference chemical (Gaucho, an imidacloprid product) was applied at 1050 g a.s./100 kg seed but the data are not included in this WoE. The study design was based on the general guidelines for evaluating the side-effects of plant protection products on honey bees (EPPO, 1992 and a method for the conduct of tunnel tests with honey bees (ANPP, 1989, revised 1996)[29]. The experimental phase of the study was conducted between 12 and 26 August 1998. Seeds were sown in tunnels with pneumatic driller in order of control (un-treated seeds, low (350), high (700), and reference (1050 g a.s./100 kg seed) on June 8, 1998. Therefore, there were four treatments each with one tunnel (136.5 m^2) parallel to the seed row. Each tunnel was divided into four zones and two zones had treated seed and two zones (refuge zones) had un-treated seed (p. 12). One hive comprising ten frames with six brood combs was placed into each tunnel. The source of the bees was identified; queens were obtained, and the miniature hives were homogeneous but a mixture of Italian or Caucasian drones. The hives each with ~10,000 bees were brought to the site on 11-12 August 1998 and placed into the tunnels on 12-14 August 1998 when the sunflowers were in bloom. Endpoints measured included mortality (number of dead bees in front of and around hive daily); foraging activity (2x daily morning and afternoon assessed as the number of bees foraging in each zone in each tunnel); flight intensity (2x daily morning and afternoon in three areas: around hive, at crop level, and elsewhere in tunnel; flight intensity was qualitatively assessed; honeybee behaviour (aggressiveness, regrouping in front of hive, resting on tunnel mesh, intense flying without foraging); colony condition on day prior to first observation and on the last day of the test (number of bees/hive, qualitative description of brood development, state of reserves, presence of healthy queens). Meteorological data were collected daily. No statistical analyses of data were conducted because there were no replicates (only 1 tunnel per treatment); however, the data in the treatment tunnels (tunnels 1 and 2) were compared to those for the control tunnel (tunnel 4) for each endpoint.	**2**

[28] Syngenta. 2000. Report on Analytical Study 100/99 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Honey and Sun Flower Heads Collected in Study 983769. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1363 - A9567B. 4 p
[29] EPPO (1992): Guideline on test methods for evaluating the side-effects of plant protection products on honey bees. EPPO Bulletin 22, 203 - 208.

	Dead honeybees were collected for residue analyses (~50 per tunnel). Sunflowers were sampled in the middle of the test and honey collected at the end of the test. No statistical analyses of the data were conducted (***major weakness***)	
Use of GLP and QA/QC.	GLP compliant with completed requirements for 1998. Study plan, deviations, and amendments were reported.	**4**
Exposure concentrations	Four treatments – two test concentrations, one experimental control and one positive reference control (Gaucho). No replicates and only one site. There were two honey samples assessed for TMX residues both of which were <LOQ of 1 µg/kg and well below the chronic NOAED of 10.6 ng/bee/d (WoE_{EXP}).	**2**
Transparency of data.	Biological data provided in summary and in appendices in tables. No residue or analytical chemistry data so no exposure data other than the nominal application rates provided.	**2**
Number of samples and replication.	Samples collected over time from each tunnel for each endpoint on at least 2 or more occasions but no independent replication.	**0**
Overall evaluation of methods		**2.00**
Score for expert judgment on quality of the study- No statistical analyses of the data were conducted (**major weakness**).	**0.5**	**1.00**

Response 1. Effects on honeybee mortality – number of dead bees		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values were presented. There was no apparent adverse effect on honeybee survival (Figure in subsection 8.2.1, p. 17; data in Appendix D).	**0**
Concentration- or dose-response	There were two applications of TMX-treated seeds (350 g and 700 g a.s./100 kg seed) with no independent replication. No concentration-response relationship was apparent.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee foraging activity		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values were presented. There was no apparent adverse effect on foraging activity of honeybees (Figures in subsection 8.1.4 and 8.2.2, p. 18-19; data in Appendices E, F, G, H and I) relative to the bees in the control tunnel and relative to the bees using the refuge areas in the treated tunnels.	**0**
Concentration- or dose-response	There were two applications of TMX-treated seeds (350 g and 700 g a.s./100 kg seed) with no independent replication. No concentration-response relationship was apparent.	**0**

Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	Flight intensity in the TMX treatments was compared to that for the control treatment. No statistical procedures were applied to these data and no P or r^2 values were presented (Table in subsection 8.2.3, p. 20). Flight intensity was similar between treatments and sporadic differences over time were attributed to weather.	**0**
Concentration- or dose-response	There were two applications of TMX-treated seeds (350 g and 700 g a.s./100 kg seed) with no independent replication. No concentration-response relationship was apparent.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No data were presented. A statement on page 20 in subsection 8.2.4 simply states that throughout the study, there was no abnormal behavior of bees observed in any treatment.	**0**
Concentration- or dose-response	There were two applications of TMX-treated seeds (350 g and 700 g a.s./100 kg seed) with no independent replication. No concentration-response relationship was apparent.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on colony condition – food stores		**Score**
Statistical significance of responses	Colonies introduced into the tunnels were healthy with a medium amount of honey reserves. Similar levels of food reserves were observed throughout the study for the four hives that were used in the test.	**0**

Concentration- or dose-response	There were two applications of TMX-treated seeds (350 g and 700 g a.s./100 kg seed) with no independent replication. No concentration-response relationship was apparent.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on colony condition – brood development		**Score**
Statistical significance of responses	Data were for the most part qualitative in nature. General observations on the condition of the colonies at the end of the study appeared to show that for the two tunnels in which seeds were treated with TMX applied at 350 g and 700 g a.s./100 kg of seed, the reduction was acceptable, particularly for the lowest test substance rate applied.	**0**
Concentration- or dose-response	There were two applications of TMX-treated seeds (350 g and 700 g a.s./100 kg seed) with no independent replication. No concentration-response relationship was apparent.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	May 17, 2016
SEJ	Yes	May 30, 2016

(Syngenta 1999)
Report: Syngenta. 1999. BeeSCAN Monitoring in Summer Rape Grown from Seed Dressed with Cruiser A 9567 B. Munchwilen, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1351 - A9567B. 48 p

The aim of the study was to determine the effects of the oil-seed spring-rape (sOSR) grown from seeds dressed with Cruiser A 9567 B on the honey bee under natural conditions in the field by using the microprocessor-controlled system "BeeSCAN" for the description of changes in flight intensity, loss of foragers and colony development.

Responses 1-10: Quality of methods			**Score**
Experimental design and hypotheses	The test methods used in this study are based on the BBA Guideline part VI, 23/1 1991 and EPPO Guideline 170[4]. The test was done at one site and comprised one treated test plot and one untreated (control) plot. The plots contained flowering *Brassica napus* or summer oilseed rape (sOSR). The treated plot was grown from seed dressed with Cruiser A 9567 B, a TMX formulated product with 70.1% purity. Control plots received no treatment. The effects of the test substance on honeybees were determined using the following criteria: mortality rates, flight activity of foraging bees, behaviour of the bees, weight of the colony, and change in Quality of the colonies and state of the brood. Methods were not well described; neither was the test substance (*weakness*). Dead bee traps and linen sheets in front of the hives were used to assess honeybee mortality. Bee activity was assessed using a BeeSCAN precision scanner at the entrance of each hive entrance and measurements were taken at 5 min intervals. Flight intensity was evaluated as number of bees foraging, resting or flying in five 1 m^2 plots per field. The number of hives used in the study was not explicitly stated; however, from the tabular data there were two colonies for each treatment (see Table 1 in Appendix 4). Measurements were made between June 14, 1999 and June 20, 1999 so the duration of the study was about one week (7 d). The origin of the honeybee colonies was provided (Appendix 5). Meteorological conditions were monitored (Figures 1 and 2; and Figures 1-2, Appendix 1). No statistical procedures were applied to the data (***major weakness***).		**2**
Use of GLP and QA/QC.	This was a non-GLP study but methods were described and generally followed those cited.		**2**
Exposure concentrations	No TMX or clothianidin residues were measured in any matrices. Seeding rates were not verified. There is no actual measure of exposure.		**0**
Transparency of data.	Raw and summary biological data were reported (except for behaviour); no analytical chemistry was included.		**3**
Number of samples and replication.	One field two plots (TMX and control) each with 2 hives; no independent replication but pseudo-replication of hives within treatments.		**1**
Overall evaluation of methods			**1.60**
Score for expert judgment on quality of the study – no statistical analyses of data comprise a **major weakness**		**0.5**	**0.80**

Response 1. Effects on honeybee mortality – number of dead bees in front of hive	**Score**

Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Figures 3 and 4 and Table II and summarized in Tables 1-2 (Appendix 1). No increase in mortality was observed during the experimental trial. No acute toxicity could be observed.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight/foraging activity		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Tables 1-2 (Appendix 1). Summary data are provided in Table III. The foraging activity results show a high presence of bees on the test plot and control plot. No difference could be observed between test plot and control.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee flight activity using BeeSCAN		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Figures 1-28 (Appendix 3) and summarized in Tables 1-2 (Appendix 4). Comparative summaries are provided in Figures 6-18. All colonies had a normal flight activity. No decrease of flight activity or an elevated rate of absolute bee loss was observed.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**

Overall evaluation of relevance (SEJ).	

Response 4. Effects on colony condition – hive weights		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Figure 19 and weights were continuously measured for one colony per treatment from June14 to June 20, 1999. During the 7-day period, the hive weight gains in the control and TMX treatment were similar at 3.1 kg, starting weight was 32.8 kg while that for the control treatment was 0 kg weight gain since the hive weight was constant at 36.2 kg.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-9. Effects on colony Quality – brood development		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Figure5 and summarized in Appendix 2. Development of broods (eggs, larvae, pupae) and food stores (honey and pollen) were similar between treatments; however, there were fewer drones produced in the control hives relative the TMX-treatment hives. The test colonies as well as the control colonies developed normally and consistent with the seasonal pattern. All colonies were containing the different stages of brood.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Bees behaved normally on both fields. The short staying of forager bees on the blossoms in both fields and the data of the electronic scales suggest less nectar flow on both fields. Bees in the field were sometimes aggressive to the study personnel. No persistent or consistent adverse effect of TMX on the behaviour of honeybees was observed.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**

Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2000b)
Report: Syngenta. 2000. Two Field Trials to Determine the Effects of HELIX™ Seed Treatment on Honeybees Foraging on Canola Flowers. Guelph, Canada: Syngenta Ltd. (Unpublished Report). Report CGA293343_1384 - A11642A. 183 p

Crop residue experiments in Alberta, Canada (p. 12) were carried out with HELIX-treated canola in 1997-1998, and the results showed that no residues were detected in the mature seed (>0.01 ppm). This study was designed to investigate if residues in flowers, pollen and nectar are sufficiently low and as such not harmful during the time when bees and other pollinating insects are active in the crop.

Responses 1-6: Quality of methods		Score
Experimental design and hypotheses	HELIX 289 FS applied as a seed treatment contains a mixture of 4 active ingredients: CGA 169374 (difenoconazole), CGA 173506 (fludioxonil), CGA 329351 (metalaxyl-M) and CGA 293343 (TMX). Two sites were selected in Canada where canola is typically grown. Site 1 was at Blackfalds near Bentley, Alberta and site 2 near Wetaskiwin, Alberta. Different canola varieties were used between sites (var. LG45A51 and LG3345, respectively for sites 1 and 2). The target application rate was 15 mL/kg of seed which was verified (Table 1) and the measured concentrations were 354 and 422 g a.s./100 kg seed, respectively. There were two sites and 15 hives placed when a minimum of 20% of the crop was flowering at each site. At each location, a plot of approx. 15 ha (36 acres) of canola was grown from seed treated with HELIX, and an adjacent 15-ha plot of canola grown from seed treated with a commercial seed treatment; VITAVAX RS (mixture of lindane, carbathiin and thiram) was planted as a reference treatment. To ensure crop foraging fidelity, the other fields around the area where the hives were placed contained grassy pasture or cereal crops. No other canola fields were within 1 km (*potential weakness*), so the bees theoretically only had access to treated, untreated and reference canola. Hives were placed at each site in 3 groups- 5 hives at the edge of the treated crop; 5 hives 20-m from southern edge in the treated crop; and, 5 hives at a reference site at least 4 km from the treated crop which served as the control group for this site (Figures 3 and 4). The hives were uniform in Quality and standard bee practices for hives were followed. All hives were found to be in good condition when inspected during setup in the field except hive No 4 in the control group at site 1, which appeared to have no active queen. The endpoints measured included: hive vigour and foraging behaviour (over 21 days) where hive vigour was determined by hive weight quantitatively and by visual inspection (qualitatively) for dead bees, brood pattern and egg laying (Tables 11-12). Foraging behaviour was assessed by comparing the number of bees in the treated plot to the number of bees in the commercial standard plot. This was used to check for any avoidance (repellence). Hive weight gain was also used as a measure of successful foraging. Tracheal and Varroa mite assays were conducted to assess colony health.	**3**

	Samples of canola flowers, pollen, honey and whole bees were collected for residue analyses (e.g., TMX and clothianidin) (Tables 21-28 and Appendix 6). Nectar samples were collected from foraging bees and from flowers. Analysis was performed using mass selective detection to minimise the possibility of incorrect identification of residues. The analysis was done using procedures with extremely high sensitivity to check for the active ingredient TMX and its major metabolite clothianidin identified from plant metabolism studies. A Turbo Ion spray LC/MS/MS was used, which provided adequate sensitivity for this study. Both TMX and clothianidin were determined in the same analytical procedure. The detection limits were 0.40, 0.2 and 0.1 µg/kg in flowers pollen and honey, respectively, and 0.02 nanograms/bee in bees. The results below the limit of quantitation, (1 µg/kg in flowers, pollen and honey and 0.10 ng/bee in bees) were too small to be measured accurately relative to the background noise of the instrument. These values were reported as trace amounts. The average recoveries for TMX were 104% and 100% on d-0 and 106% compared 81% on d-133 for honey and honeybees respectively. The average recoveries for clothianidin on d-0 were 74% and 87% compared to 74% and 78% on d-133 for honey and honey bees respectively. Source of hives was not identified. Sites were detailed and characterized (Table 2) and soils characterized (Table 3). A local weather station provided meteorological data (Tables 7-10; Figures 5-6). Land use history was provided (Tables 4 and 5). Methods used to collect data and samples were described in detail. Storage and sample handing were provided and the statistical procedures applied to the data (only the hive weights – **a major weakness**) described. A conservative hypothesis of no adverse treatment effect on the hives was used, with a one-tailed t-test, at the 90% confidence level. Groups of hives at the edge of the field or in the treated canola field were assessed separately after two time intervals. Planting dates and information were included (Table 6).	
Use of GLP and QA/QC.	GLP study complete with signatures, QA certificate, study plan, deviations and amendments. Analytical chemistry was GLP. Purity and stability of test substance was established. Seed loading were confirmed (Table 1).	**4**
Exposure concentrations	A similar concentration of TMX was used at each of two sites which were independent replicates. Analytically confirmed loading and drilling rates. Residues were measured in pollen and honey (see WoE_{EXP}).	**4**
Transparency of data.	Raw data and summary data provided.	**4**
Number of samples and replication.	Samples collected were adequate but there were only two treated sites and two control sites.	**2**
Overall evaluation of methods		**3.40**
Score for expert judgment on quality of the study - no statistical analyses of data was a **major weakness**	**0.5**	**1.70**

Response 1. Effects on colony Quality – hive vigor or weight gain		**Score**
Statistical significance of responses	Weight gain was found to be the best quantitative measure of hive vigor. The hives gained weight rapidly and no treatment-related effect was found (Table 19 and 20; P >0.05).	**0**

Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-4. Effects on foraging/flight activity or honeybee behaviour		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Tables 13 and 14. There were no observable effects on bee foraging activity, no evidence of repellency, loss of co-ordination or disorientation. Bees were observed foraging in the HELIX-treated crop area around the hives, and did not avoid it in favour of other available pollen and nectar sources.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Tables 11 and 12. No treatment-related dead bees were found.	**0**
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on colony Quality – brood development		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. Data are provided in Tables 11 and 12. Both exposed and unexposed hives thrived and grew, except for one control hive at site 1, which was weak and had no egg laying. There was no apparent	**0**

	adverse effect on brood pattern or egg laying with respect to the TMX treatment.	
Concentration- or dose-response	There was only one application of TMX-treated seeds; therefore, a concentration-response relationship is not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

The results showed that the bees were not affected by the Helix Treatment. Both exposed and unexposed hives thrived and grew, except for one control hive at site 1, which was weak and had no egg laying. Bees were observed foraging in the HELIX-treated crop area around the hives, and did not avoid it in favour of other available pollen and nectar sources. There were no observable effects on bee foraging activity, no evidence of repellency, loss of co-ordination or disorientation. No treatment-related dead bees were found. There was no apparent adverse effect on brood pattern or egg laying. The bees from all hives in the exposed groups were actively foraging in the HELIX-treated canola. Bee mortality was low and not related to the treatment. Weight gain was found to be the best quantitative measure of hive vigour. The hives gained weight rapidly and no treatment-related effect was found (Table 19 and 20).

The pollen and honey collected at the HELIX-exposed hives contained insignificant traces (1 ppb or less) of parent compound and no detectable degradate. The foraging bees and the returning bees collected at the hive entrance contained traces of parent compound and occasional traces of the degradate (< 0.05 and <0.03 ng/bee respectively). The oral LD50 of thiamethoxam in bees is 5 ng/bee (Testing Toxicity to Honeybee – *Apis mellifera* L. With CGA – 293343. Report No. 742-95. R. Kleiner, BioChem GmbH, Karlsruhe, Germany. Oct 24, 1995. DACO 9.2.4.2 Co. No. 9.2.4.2.1. Unpublished report submitted Dec 4, 1998). This is 250 times higher than the detection limit and more 100 times above the highest levels found in foraging bees.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2000g)
Report: Syngenta. 2000. Tunnel Test- Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 70 WS (A-9567 B) on Honey Bees (*Apis mellifera*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1408 - A9567B. 123 p

and

(Syngenta 2000d)
Report: Syngenta. 2000. Report on Analytical Study 107/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads), Honey, and Pollen Collected in Study S99NCB1556V046. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1366 - A9567B. 6 p

The aim of this semi-field study was to assess the effects of sunflowers (*Helianthus annus*) grown from TMX-treated seed (70 WS) on honeybees (*Apis mellifera*) under field conditions following the EPPO guideline No. 170[4] using tunnels to house the bee colonies. A weight of analysis of the effects data are summarized herein.

Responses 1-5: Quality of methods		**Score**
Experimental design and hypotheses	The bees were exposed to sunflowers (var. Cadasol) grown from TMX treated seed (TMX at nominal 350 g a.s./100kg seed and Quinolate Pro FL at 0.25 L/100 kg seed) sown (95,000 seeds/ha or 7.41 kg/seed/ha) on May 28, 1999 in tunnels at a farm near Merainville in Beauce area in southern France. The experimental control used seed treated with Quinolate Pro FL and the positive control used Gaucho WS (imidacloprid) + Quinolate Pro FL at nominal loadings of 1050 g a.s. imidacloprid/100 kg seed, and a foliar application of dimethoate. There were 10 tunnels distributed across 4 treatments: 4 for the untreated control treatment; 3 for the TMX treatment; 3 for the Gaucho treatment; the extra tunnel in the untreated control received a foliar application of dimethoate (Figure 1). There was a single site with 10 established plots each consisting of four zones. Each plot was at least 6 m from the adjacent plot. Hives were installed in each of the three or four tunnels on each treatment plot. Honeybees (*Apis mellifera mellifera*) were healthy and were from a local commercial source. Each hive contained approximately 10,000 bees. The hives were placed in the tunnels on 1999-07-23at flowering stage BBCH 58/59. Hives remained in place until 1999-08-11. Measurement endpoints included honeybee mortality, foraging activity, honeybee behaviour, flight intensity (duration of flower visits), colony Quality (food stores – honey and pollen), colony Quality – brood development. Samples of soil, dead bees, bee pollen and flower heads and nectar, and honey were collected for residue analyses. Source and supplier of bees was provided and the preparation of hives described in detail. Soil was characterized (p. 18); pesticide historical use and land use was provided (p. 18; Table 2); meteorological conditions were provided.	**2**

	Statistical procedures were applied to the data and described in detail (see subsection 3.11, p. 24-25).	
Use of GLP and QA/QC.	GLP study (with signatures missing), QA assurance, study plan, deviations, amendments etc. were provided.	**4**
Exposure concentrations	There was only one application rate of the TMX-treated seeds. The test item was applied at the following rate: 367,4 g a.i,1 00 kg seed (104.97% of the nominal rate of 350 g a.s./100 kg seeds) in mixture with Quinolate Pro Fl (0.25 L/100 kg seeds). Residue data were provided elsewhere (see above) and TMX residues in sun flower heads (n = 3), honey (n = 3) and pollen collected by bees (n = 9) were <LOQ of 1 µg/kg.	**1**
Transparency of data.	Raw and summary data were included but some were not legible. No residue data were included in this report, just the list of samples collected, however residue results are provided elsewhere (see above).	**3**
Number of samples and replication.	There was only one application rate of TMX used as a test substance and one as a positive control. A negative control was used as well. There were three tunnels per treatment but they were not independent replicates as the tunnels were at the same site.	**2**
Overall evaluation of methods		**2.40**
Score for expert judgment on quality of the study	**1**	**2.40**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	Mortality data are summarized in Table 1 and in the Appendix, Table 7 (Graph 1). The cumulative mean number of dead bees in each treatment was 7900, 7460, 4735, and 7549, respectively for the control, TMX, imidacloprid and dimethoate treatments. There was no significant difference in mortality between the control and the TMX treatments (ANOVA, Dunnett's; p >0.1).	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration- response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on foraging activity of honeybees		**Score**
Statistical significance of responses	A summary of the foraging activity of honeybees is provided in Table 8, Graph 2. Foraging activity increased in all treatments with an increase in the number of flowers blooming. Foraging activity ranged between 2.17 and 12.22 bees/m^2 for the controls and between 3.25 and 16.44 bees/m^2 for the TMX treatment. There was no significant difference between these treatments (p >0.07) during the exposure period; however, when the data for the entire study period were considered, significantly more foragers were reported for the TMX treatment relative to the control (p = 0.0093).	**4**

Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration- response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Increased foraging activity of honeybees might or might not adversely affect apical endpoints. There was no comment on the significance or relevance of this observation. The high variability in the colony development (Quality & brood development) precluded definitive conclusions and was a source for uncertainty.	**2**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**2.00**
Overall evaluation of relevance (SEJ). An increase in foraging would normally be considered beneficial if there were no negative effects on apical endpoints at the level of the hive. Since there were no apparent adverse effects at the level of the hive, the score was adjusted by a multiplier of 0.5.		**1.0**

Response 3. Effects on the number of honeybees entering and leaving the hive		**Score**
Statistical significance of responses	No statistical analysis was conducted for the data in Table 9 which were summarized in Graphs 3a and 3b. The number of honeybees entering and leaving the hives was similar among treatments. There were no apparent differences between the TMX and the control treatments.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration- response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	Observations of honeybee behavior were recorded during assessments of mortality, foraging, bees leaving or entering the hive or during sample collection; however, the data were qualitative and no statistical analysis was conducted. The data reported in Table 11 suggest that the honeybee behavior in the TMX treatment was similar to that for the control treatment.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration- response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on the colony Quality – brood development		Score
Statistical significance of responses	The data collected for colony condition and brood development were highly variable (Tables 14 and 15) and the data were inconclusive. For example, one of the control hives was in exceptional condition and productive, the second one was considered neither exceptional nor poor, and the third hive had no brood development. The variability associated with hives in the TMX was also high.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration- response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The high variability precluded drawing definitive conclusion of no effect and there was no speculation on potential explanatory variables (i.e., influence of other factors). The high variability persisted throughout the study so brood development and colony Quality was thought not to be related to the TMX treatment.	**0**
Mechanism and or mode of action of effect explained	No mechanism was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the test item treated crop.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2001g)
Report: Syngenta. 2001. Assessment of Side Effects of CGA 293343 + CGA 329351 + CGA 173506 FS 321.3 (A 9807 C) Applied as Seed Dressing of *Brassica napus* on the Honeybee *Apis mellifera* L. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA173506_5395 - A9807C. 59 p

And

(Syngenta 2001d)
Syngenta. 2001. Report on Analytical Study 112/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Oil Seed Rape (Flowers), Honey, Honey Stomach Content, and Pollen, Collected in Study 00 10 48 016. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1832. 6 p

The aim of the study was to evaluate the effects of TMX-treated spring oilseed rape on honeybees with a focus only on potential effects. Exposure is summarized in WoE_{EXP} and the supporting analytical report[30]

Responses 1-6: Quality of methods		Score
Experimental design and hypotheses	The field-study was conducted Germany near Leipzig (Sachsen). There were two fields, a treatment (1.59 ha) and a control (1.14 ha) which were 5 km apart. Spring oil seed rape (sOSR) (*Brassica napus* var. Forte) was treated with TMX as a formulation A-9807 C which also contained the fungicides metalaxyl-M and fludioxonil. Loading rate on seeds was measured at 401.2 g TMX/100 kg seeds; the nominal application rate was 8 kg seed/ha (verification – Table 3). No other pesticides were used on the sOSR after sowing until the end of flowering and removal of bees from the trial; historical use of neonicotinoids was not provided (*weakness*). Seeds in the treated and control fields were sown with a pneumatic seeding machine by pneumatic seed drill Accord + electronic sowing control on April 10, 2000. A reference chemical was not used. Meteorological conditions were recorded during the study and combined with data from local weather stations (Appendix 2). Twelve hives were used in the study, six in each of the test and control. Honeybees (*Apis mellifera*) were from a local commercial source and were healthy. Each colony contained 11 frames with 6-10 frames occupied with brood in the different stages; one honey and pollen super: 11 frames including 10 constructed honey combs and one foundation were provided to give enough space for bees, honey and pollen. The number of worker bees ranged from 60,000-80,000 per colony. The hives were placed in the fields when the sOSR was flowering BBCH-code: 61 (2000-06-05/06 for treatment and control, respectively). The biological measurement endpoints included: mortality (dead bees in the trap, around hives and in the field); flight/foraging intensity in the	**3**

[30] Syngenta. 2001. Report on Analytical Study 112/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Oil Seed Rape (Flowers), Honey, Honey Stomach Content, and Pollen, Collected in Study 00 10 48 016. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1832. 6 p

	field; amount of collected pollen; brood status; behaviour of bees; and, weight of hives using standard practices that were described in detail. The brood status (number and covered area/comb with eggs, larvae, sealed cells, empty cells, honey cells or pollen cells) was assessed 48 h before (2000-06-08), 19–20 days after (2000-06-28/29), and 7 weeks after exposure (2000-07-27). Mortality was assessed daily using dead bee traps and linen sheets in front of the hives and on 3 linen sheets (0.5 x 10 m) distributed around each field. Foraging activity was assessed daily on 3 small plots (1 x 10 m) distributed around each field. Mortality and foraging activity were assessed during the 17-d exposure period. Statistical procedures were applied to the data and described (Appendix 1; Subsection 2.5).	
Use of GLP and QA/QC.	This was a GLP study. The effects component and the analysis of residues were conducted under GLP with QA. Weather data were not recorded under GLP. Collection of the nectar from the forager bees was in the spirit of GLP. Biological methods were those recommended and standard practice at the time.	**4**
Exposure concentrations	Rate of application of the seeds was verified (401.2 g TMX/100 kg seeds); only a single concentration was used. Residues measured in nectar and pollen collected from foraging bees were low as was that in honey collected from the hives (WoE_{EXP}).	**4**
Transparency of data.	All raw data were provided.	**4**
Number of samples and replication.	There was only one site per treatment but there were six pseudo-replicated hives per site.	**1**
Overall evaluation of methods		**3.20**
Score for expert judgment on quality of the study	**1**	**3.20**

Response 1. Effects on honeybee mortality – dead bee traps & linen		**Score**
Statistical significance of responses	The mortality of bees was low in the colonies of both treatments (TMX and control). Over the 17-d assessment period, no increased number of dead bees was observed for the TMX treatment compared to the control treatment for either the DBT or linens (Table 6). For the field assessment areas, there was also no significant difference between treatments. There was no obvious statistically significant mortality (Appendix 1; n = 28; P>0.05) observed for any bee hive (in the trap), around hives and in the field over the whole test period of 17 days.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration-response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**

Overall evaluation of relevance (SEJ).	

Response 2. Effects on foraging activity		**Score**
Statistical significance of responses	The flight activity in the TMX-treated plot was similar to that for the control plot (Table 7). The number of foraging bees on the blooming oilseed rape in the TMX treatment was similar to that in the control. This was corroborated by the fact that there was no statistically significant difference in the average amount of pollen collected per colony between control and test item colonies during 17 days of assessment (Table 8 and Appendix 1). The observed differences concerning number of foraging bees/plot and amount of collected pollen were in a normal range of the biological variability between treatments.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration-response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No abnormal behaviour of bees during foraging on rape flowers was observed; however, quantitative data were not provided. Observations were made concurrently with collection of mortality and foraging data.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration-response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee colony Quality - # honeybees		**Score**
Statistical significance of responses	No adverse effects on population density of TMX exposed colonies compared to control colonies were observed during two brood assessments during the monitoring phase (post-exposure). This statement was not supported by statistical analyses of data.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration-response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**

Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on honeybee colony Quality – brood development		**Score**
Statistical significance of responses	No adverse effects on brood development and population density of the TMX exposed colonies (Table 9) compared to control colonies were observed during two brood assessments after field exposure termination. The results of the brood assessments for the TMX-exposed colonies with a mated queen indicated colonies with well-developed brood nest including 3 to 10 brood covering combs over the whole test period. One colony (#5) swarmed and reared a new queen which produced less brood during until the 3rd assessment. No statistical analyses of these data were included.	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration-response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on honeybee colony Quality – hive weights		**Score**
Statistical significance of responses	There was no significant difference (decrease) in hive weight between treatment colonies at the end of the test (Table 10). Only two of six hives in the control and one of six hives in the treated plot were slightly but not significantly lighter at the end of the field exposure phase (Appendix 1; p = 0.808 and 0.942, respectively).	**0**
Concentration- or dose-response	A single application of TMX-treated seeds was used so an exposure concentration-response relationship was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	May 19, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2001h)
Report: Syngenta. 2001. Field Test: Side Effects of Oil-Seed Winter-Rape Grown from Seeds Dressed with Cruiser® OSR (A9807 C) on the Honey Bee (*Apis mellifera* L.). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA173506_5423 - A9807C. 80 p

The effects of TMX-dressed oil-seed winter-rape (wOSR; *Brassica napus*) (1.5 L Cruiser® OSR per 100 kg seeds) on the honey bee (*Apis mellifera* L.) was assessed under field conditions in southern Germany near Pforzheim (Figure 6). The risk associated with residues in bee-relevant matrices was evaluated in a WoE_{EXP} based on Report CGA293343_1830[31].

Responses 1-12 Quality of methods		Score
Experimental design and hypotheses	There were two fields (3.94 and 4.28 ha) separated by 3 km for the TMX treatment and the control treatment, respectively. One was planted with TMX-treated wOSR (var. Express) and the other with TMX-free seed (var. Express). The TMX sowing rate was 4.20 kg seed/ha (measured 416 g TMX/100 kg seed) and the application rate was 63 mL CRUISER® OSR/ha whereas the sowing rate for the control field was 4.01 kg seed/ha (Table 2). Different machines were used for drilling seeds. Six hives were placed into each field at the edge in two groups of three separated by 30 m prior to full flowering (BBCH-59-60) on April 20, 2000. Three colonies were equipped with dead bee traps (DBTs) at the hive entrance six days after colonies were placed in the fields. Linen sheets (each 5 m^2) in front of the hives and at three assessment areas in the field were also used to assess mortality. Observations for flight intensity took place in five marked areas (each 1 m^2) 3-times daily for 8 d along with foraging activity and honeybee behaviour which were evaluated between d-6 and -13 after setup. Colony condition and brood status was evaluated every 8 (±1) days during the complete flowering period on d 5-6, 12, 20, and 49, after setup. Methods cited included EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]. The certified healthy hives were of similar size and Quality and contained 2-3 brood bodies with at least 8 brood frames and at least 19 honey frames and the number of bees ranged from 30,000 to 40,000 worker bees per colony. Source of bees was reported. At the end of flowering the exposure phase May 10, 2000, the colonies were relocated to Kőnigsbach-Stein for monitoring. Meteorological data were recorded; temperature, relative humidity, rainfall and weather conditions from a weather station (non-GLP) 2 km from the study site. Methods for biological data collected were described in detail in Subsection 4.5 and summarized in Tables 3-5. Endpoints measured included mortality (daily), flight intensity (three times a day) between d-6 and -13 after the hives were set up, and	**3**

[31] Syngenta. 2001. Report on Analytical Study 102/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Winter Rape (Leaves, Blossoms), Honey, Honey Stomach Content, and Pollen, Collected in Study 99393/01-BFEU. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1830. 6 p
[32] SETAC (1995): Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides. M. R. Lynch (Ed.), 49-51

	condition of the colonies and brood development (every eight days starting on d 5/6 after setup) on four separate occasions (see above). Colony Quality included the # of combs covered by bees, the presence of health queens (eggs & queen cells), the comb area with food storage (pollen & nectar) and brood development (comb area with eggs, larvae, and capped cells). Hive weight was measured daily on one colony in the first of group of three hives for each treatment using a beam-scale. Weights were recorded at night when the bees were in the hive. The increase or decrease of the remaining two colonies of the group were recorded on the individual days of brood appraisal using a beam scale (i.e., April 25/26, May 9/10). Honeybee behaviour, in front of the hive and in the field, was observed. Dates for activities and events are summarized in Tables 3-5. Statistical procedures were applied to the mortality data, only and not for the other endpoints (***major weakness***). Assumptions were tested and either parametric or non-parametric procedures were used and a pre-determined significance level of p≤0.05. Samples of plant material (leaves and flowers), contents from foraging honeybee stomachs, nectar and honey from the hives were collected for residue analyses which was not reported in this study but was reported elsewhere[40]. One honey comb from the second group of three hives in each treatment was removed, placed into the plastic bag and frozen (-18ºC) for potential residue analyses. The comb was replaced with a new one each time (see subsection 4.6.1). The sampling methods for honeybee stomach content, plant material & soils, and collection of dead bees for potential residue analyses are described in subsections 4.6.2, 4.6.3, and 4.6.4, respectively.	
Use of GLP and QA/QC.	GLP study with statement of QA, study plan deviations and amendments, signatures; certified analytical lab.	**4**
Exposure concentrations	A single application rate was used for the TMX treatment. No residue data were included. The application rate was verified. TMX residue concentrations in hive honey (n = 18), nectar (n = 5) or pollen (n = 1) from bees were <LOQ of 1 µg/kg and well below the chronic NOAED of 10.6 ng/bee/d.	**4**
Transparency of data.	Raw and summary data were included.	**4**
Number of samples and replication.	There were two fields, one treatment and one control. There were 6 hives in 2 groups of three per treatment (pseudo-replication) and multiple measurements (repeated measures) collected over time.	**1**
Overall evaluation of methods		**3.20**
Score for expert judgment on quality of the study- statistical procedures were only applied to the mortality data **(*major weakness*).**	**0.5**	**1.60**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	The mean mortality (number of dead bees/colony/day) in TMX treatment was slightly higher over the entire observation period (DAE 6 to DAE 13) compared to the mean mortality in the control treatment (Figure 1; TMX group: 13.3 - 35.7 dead bees/colony/ day; control group: 1.7 - 8.3 dead bees/colony/day); however, it was significantly higher (p≤0.05) only on DAE 7 after hive set up (Table 6). There was	**4**

	no significant difference for mortality of honeybees on linens between treatments (Table 14-15; Appendix A2).	
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The average daily mortality was within the normal range expected for bee colonies, regardless of TMX exposure. This could be considered a temporary impact with no consistent trend with little impact on the apical endpoints at the end of the season (October 2000).	**2**
Mechanism and or mode of action of effect explained	The significant increase in mortality on DAE 7 in the TMX treatment might have been caused by a higher foraging activity of the bees in the test item field compared to those of the control field.	**2**
Overall evaluation of relevance (computed)		**2.67**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P values or r^2 values reported. The flight intensity (mean foragers/m^2/d) was comparatively low in both treatment groups (0.2 to 1.3 bees/m^2 in the TMX treatment group; 0.1 to 0.4 bees/m^2 in the control treatment group) throughout the entire test period (DAE 6 to DAE 13); however, the flight intensity was higher in the TMX field compared to that in the control field (Figure 2; Tables 16-17, Appendix A2). The average flight intensity in the TMX-treated field was 0.6 bees/m^2/day compared to 0.3 bees/m^2/day in the control field (Tables 16–17, Appendix A2). Variability was high for both treatments.	**2**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since test fields were of a size of approximately 40,000 m^2, the total number of forager bees ranged from 8,000–52,000 bees/field/day in the TMX treatment compared to 4,000–16,000 forager bees/field/day in the control.	**2**
Mechanism and or mode of action of effect explained	This indicates that the bees were actively foraging in both fields, but much more in the TMX-treated field compared to the control.	**2**
Overall evaluation of relevance (computed)		**2.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on colony Quality – hive weights		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. No difference in the weight gain over the assessment period could be observed between TMX and the control treatment (weight gain was between 18.2 and 23.4 kg in the control colonies and between 17.1 and 21.3 kg in the TMX colonies (Tables 7-8).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**

Overall evaluation of relevance (computed)	**0.00**
Overall evaluation of relevance (SEJ).	

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. There were no significant differences in honeybee behavior for the two treatments. Foraging and pollen collection behavior was observed to be normal for both treatments (Tables 25-26, Appendix A2). On all evaluation days, no abnormal behaviour of the bees on the crop and around the colonies in both treatments was observed.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-12. Effects on colony Quality – # combs with bees, presence of health queens (eggs & queen cells), food storage (pollen & nectar) and brood development (comb area with eggs, larvae, and capped cells)		**Score**
Statistical significance of responses	None of the six colonies of the TMX treatment (Figure 3) experienced a significant decrease in the Quality of the colonies or bee brood development compared to the control groups (Figure 4) by the last brood assessment period and the number of combs covered by bees ranged between 17 and 22. The presence of eggs at the last brood assessment showed that the queens were in good condition in all colonies of the treatment groups. Variability was relatively high among hives within treatments (Tables 18-21, Appendix A2). In hive 1 of the TMX group, no eggs were observed at the 1st and 2nd brood assessment (Figure 3). This was thought to be due to the damage of the queen at the transport of the hive to the test location or the bees had swarmed before the first brood assessment. The area on combs covered with brood was reduced in all colonies of both test groups compared to the area on combs covered with nectar and pollen (see Figures 3 and 4, and Tables 18-21 in Appendix A2). Since flowering wOSR is an attractive source for nectar and pollen for bees, the main comb area was used for storage of food.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**

Overall evaluation of relevance (computed)	**0.00**
Overall evaluation of relevance (SEJ).	

Narrative
There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the test item treated crop.

Expert Judgement		
QA	Yes	May 18, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2001i)
Report: Syngenta. 2001. Field Test (Non-GLP): Side Effects of Oil-Seed Winter-Rape Grown from Seeds Dressed with A9807 C on the Honey Bee (*Apis mellifera* L.). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA173506_5452 - A9807C. 37 p

The effects of TMX-dressed winter oilseed rape (wOSR; *Brassica napus*) (1.5 L Cruiser® OSR per 100 kg seeds) on the honey bee (*Apis mellifera* L.) was assessed under field conditions in southern Germany near Stuttgart (Figure 3, Appendix 1).

Responses 1-13 Quality of methods		Score
Experimental design and hypotheses	There were two fields (6.0 and 6.0 ha) separated by 7 km for the TMX treatment and the control treatment, respectively. One was planted with TMX-treated wOSR (var. Express) and the other with TMX-free + fungicides seed (var. Express) on August 26 and 27, 1999, respectively. The TMX sowing rate was 400 g a.s./100 kg seed (actual 416 g) and the application rate was 63 mL CRUISER® OSR/ha; sowing rate for the control field was not measured but was similar to the 4.0 kg seed/ha for the treated plot (Table 1). A pneumatic seeding machine was used (Amazone D/30 Super S). No other plant protection products were used in this study; historical use was not provided (*weakness*). Nectar secretion of rape flowers was measured. Four queen-right and certified healthy hives were placed into each field at the edge of the field prior to full flowering (BBCH-59-60) on April 18, 2000. Three colonies were equipped with dead bee traps (DBTs) at the hive entrance and the fourth colony was similarly situated but had no DBT. The number of dead bees in front of the hive was also recorded. Mortality was measured in the morning for 31 d (from April 20th to May 19th, 2000) and dead bees were removed from the traps and in front of the hive. Flight intensity of honeybees was measured in two areas in the field (each 4 m^2) twice a day for 8 non-consecutive days starting on April 20th 2000 and ending on May 8th, 2000 (Table 3), when the number of foraging bees was recorded. Colony condition and brood development of all four hives were assessed on four occasions during the flowering period (Tables 2 and 3) starting 2 days after exposure and ending on May 10th, 2000. Honeybee behaviour was evaluated concurrently with observations on mortality and foraging or flight activity. Hive weights were measured continuously on three colonies in each treatment using a beam scale; however, the data when bees were in the hive were compared over time. Methods cited included EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]. The certified healthy hives were of similar size and Quality and contained 3 bodies (without queen excluder) with at least 10 brood frames and 4 honey combs. The number of bees was approximately 30,000 worker bees per colony. Source of bees was reported. Meteorological data were recorded; temperature, relative humidity, rainfall and weather conditions from a weather station (non-GLP) 1.5 km from the study site (Tables 5-7). Methods for biological data collected were described in detail in Subsection 5.5 and summarized in Tables 2-3. Endpoints measured included mortality (daily for 31 d), foraging activity, number of forager bees in the field, behaviour of honeybees, colony Quality (# of combs covered by bees, the presence of health queens	**2**

	(eggs & queen cells), the comb area with food storage (pollen & nectar) and comb area with eggs, larvae, and capped cells. Hive weight and nectar secretion of rape flowers. No statistical procedures were applied to endpoints (***major weakness***). No samples were collected for residue analyses and no residue data were included in this report (***major weakness***).	
Use of GLP and QA/QC.	This was not a GLP study; however, the methods were reasonably described. No QA or QC.	**2**
Exposure concentrations	A single application rate was used for the TMX treatment. No residue data were included. The application rate was verified.	**1**
Transparency of data.	Raw and summary data were included.	**3**
Number of samples and replication.	There were two fields, one treatment and one control. There were 4 hives/field (pseudo-replication) and multiple measurements (repeated measures) collected over time.	**1**
Overall evaluation of methods		**1.80**
Score for expert judgment on quality of the study- no statistical procedures were applied to the data which is a **major weakness.**	**0.5**	**0.90**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical analyses of the data were performed and no P or r^2 values were reported. The average daily mortality from days 2-31 was 21.8 dead bees/colony in the TMX treatment compared to 22.1 dead bees/colony in the control (Tables 8 and 9, Appendix A2). For the most part during the exposure phase (days 4-15), mortality was higher in the control colonies (Figure 1) which was attributed to other causal factors (fungal disease, p. 15).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee foraging activity & intensity		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P values or r^2 values reported. Throughout the entire test period an average of 5.0 forager bees/4 m^2/day were recorded in the TMX treatment compared to 2.4 forager bees/4 m^2/day in the control field (Figure 2). No effect was observed concerning the number of bees which were actively foraging on the test item treated crop.	**0**

Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on colony Quality – hive weights		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. No difference in the weight gain over the assessment period of individual hives (Table 4) was apparent between those in the TMX and the control treatment (the average weight gain was 19.5 and 16.4 kg for the TMX and the control colonies, respectively) (Table 4).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	There were no data presented for behaviour, no statistical procedures were applied, and no P or r^2 values were reported. There were no significant differences in honeybee behavior for the two treatments (Subsection 7.4)	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-12. Effects on colony Quality – # combs with bees, presence of health queens (eggs & queen cells), food storage (pollen & nectar) and brood development (comb area with eggs, larvae, and capped cells)		Score
Statistical significance of responses	No statistical analyses of the colony Quality data were conducted and no P or r^2 values reported. The results for the assessments for individual hives are summarized in Tables 12 and 13, Appendix 2). Variability was high within the control colonies because one colony lost the queen by the second assessment and no brood developed. Otherwise, brood development was normal over the period of assessments and no treatment effects were apparent.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 13. Effects on nectar secretion of rape flowers		Score
Statistical significance of responses	No statistical analyses of the colony Quality data were conducted and no P or r^2 values reported. The number of flowers with nectar-drops on the nectar glands was equal in both treatments with an average of 0.5 - 10.0 flowers with nectar/10 flowers/day in the TMX treatment compared to 0.0 - 10.0 flowers with nectar/10 flowers/day in the control field (Tables 16 and Table 17, Appendix A2). The average number of flowers with nectar during the entire test period was 5.1 and 6.0 flowers with nectar/10 flowers/day in the TMX and control treatments, respectively.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2001j)
Report: Syngenta. 2001. Field Test: Effects of Oil-Seed Spring-Rape Grown from Seeds Dressed with CGA 293343 WS 70 (A 9567 B) on the Honey Bee (*Apis mellifera* L.) (Conducted in Northern Germany near Celle). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1360 - A9567B. 98 p

The field study was carried out according the EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]. The effects of spring oilseed rape (sOSR) dressed with 0.6 kg TMX (A 9567 B) per 100 kg seeds (sowing rate: 5.94 kg seed/ha, application rate: 0.03564 kg TMX as Cruiser WS 70 (A 9567 B)/ha) were tested on the honey bee (*Apis mellifera* L.) under field conditions in the north of Germany near Celle near Hetendorf. This study is similar to that describe for the one conducted in southern Germany[33].

Responses 1-11: Quality of methods		**Score**
Experimental design and hypotheses	Two fields were established; one for each treatment (TMX and Control). TMX-dressed sOSR (var. Licosmos) was sown in the TMX field (1.9 ha) and TMX-free sOSR (var. Licosmos) was sown in the control field (2.5 ha); seeding rates for the TMX and control fields were 5.94 kg and 7.09 kg seeds/ha, respectively. The nominal loading rate of 0.4206 kg a.s./100 kg seed was verified to be 0.432 kg a.s./100 kg seed. Loading rates were confirmed and a certificate of analysis provided (Appendix 11). The fields were in southern Germany near Pforzheim and were separated by forest and a distance of 2 km (Figures 10-13). Assessment dates and activities are provided (Table 3-5). The drilling machine was Amazone D7 Typ 30 for both treatments. Flower development was monitored (Appendix 6). Meteorological data were collected and reported; weather station was 68 km from test site. Six certified-healthy, queen-right colonies were placed into the treatment fields prior to flowering (BBCH 60) on June 11, 1999 in two groups of 3. Each colony contained 1-2 brood bodies with 6-8 brood frames and one honey body with at least 8 frames. The first group of three hives were fitted with dead bee traps. Linen sheets (5 m^2) were also established in front of the hives and in three places in the field to monitor dead bees. The second group of three hives were located 30 m from the other group and were used primarily for the collection of honey stomachs of foraging bees and the pollen. The number of dead bees found in front of the hives on the linen sheet and in the dead bee traps was recorded and the dead bees were removed once a day, in the morning, during a period of 9 d, starting 3 d after the hives were introduced. Foraging activity and flight intensity were measured three times per day in 5 assessment plots of 1 m^2 starting three days after setup for a period of 9 d. Honeybee behaviour was evaluated during the assessment period in front of the hive and in the field. Starting four days after the beginning of exposure until the end of flowering, colony condition and brood status were evaluated every 8 d (±1). The last check was 4 weeks after the end of flowering (July 27, 1999) (Tables 3-5). Hive weights were measured at specific time periods during brood appraisal and one hive in each	**3**

[33] Syngenta. 2001. Field Test: Effects of Oil-Seed Spring-Rape Grown from Seeds Dressed with CGA 293343 WS 70 (A 9567 B) on the Honey Bee (*Apis mellifera* L.) (Conducted in Southern Germany near Pforzheim). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1376 - A9567B (99125/01-BFEU). 95 p

	treatment (Group 1) was on a beam scale and weights were recorded continuously. Methods cited included EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]. The hives were removed from the test sites on June 29, 1999 and returned to the apiary (garden of the Niedersächsisches Landesinstitut für bienenkunde) for monitoring; therefore, the duration of exposure was 18 days and the last brood assessment was done on July 27, 1999 on day 46 after the first day of exposure (Tables 3-5). Source of bees was reported. The endpoint measurements included mortality, flight intensity/foraging activity, colony condition and brood development (comb area with bees, presence of health queen and queen cells, comb area with pollen and nectar, comb area with eggs, larvae, capped cells), and honeybee behaviour. Hive weights were also measured continuously with a beam scale in the first group. Methods were well described in Subsection 4.5 and standard for the industry at the time. Comparisons were made between the results for the control and the TMX treatments; however, no statistical procedures were applied to the data (***major weakness***). No P values or r^2 values were reported. Samples of plants and their pollen, soils, the contents of honey bee stomachs of the foraging bees, and newly collected nectar and honey were collected from the hives during the study, for possible subsequent chemical analysis (Subsection 4.6 for method description). Also, the pollen out of the pollen traps was collected for possible subsequent chemical analysis. Collection methods were described in detail in subsections 4.5.5. Honey was characterized (Subsection 4.6.4).	
Use of GLP and QA/QC.	The study complied with GLP with QA provided. Study followed guidelines for test methods provided by EPPO (1992)[29] and SETAC (1995)[32]. Study plan, deviations, and amendments were included.	**4**
Exposure concentrations	Application rate on the seed was verified. Although samples were collected for residue analyses; no residue data were reported. As this study was conducted in an open field, analysis of bee-relevant matrices was necessary to properly evaluate effects.	**0**
Transparency of data.	Raw and summary data were included; no behaviour data were included	**3**
Number of samples and replication.	There was only one site per treatment but there were six pseudoreplicated hives per site, which were sampled in two groups of three. Repeated measures on pseudo-replicates were made over time and the sample sizes varied depending on the endpoints.	**1**
Overall evaluation of methods		**2.20**
Score for expert judgment on quality of the study- no statistical analyses of data (**major weakness**).	**0.5**	**1.10**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values provided. During the evaluation period, daily mortalities ranged from 5.0 to 95.3 and from 1.7 to 29.3 dead bees/h for the TMX and the control treatments, respectively (Figure 2). The average mortality was 22.5 and 7.8 dead bees/colony (Figure 1), respectively. When the	**4**

	mortality attributed to bee robbery (Figure 2) is excluded, the average mortality between treatments was similar.	
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**1.33**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity/foraging activity		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P values or r^2 values reported. Throughout the entire test period an average of 14.6 bees/m^2/day were recorded in the TMX treatment compared to 12.7 forager bees/m^2/day in the control field (Figure 3). During the first three assessments (3-6 DAE), the average flight intensity was between 18.7-19.3 and 11.7-16.1 bees/m^2 flowering OSR for the TMX and control treatments, respectively; this suggests that flight intensity was significantly greater in the TMX exposed bees. This might have been a short-lived (e.g., transient) difference not confirmed by statistical procedures.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on colony Quality – hive weights		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. No difference in the weight gain over the assessment period of individual hives (Tables 10 and 11) was apparent between those in the TMX and the control treatment.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**

Overall evaluation of relevance (SEJ).	

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. There were no significant differences in honeybee behavior for the two treatments (Subsection 7.5); no abnormal behaviour was reported.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-11. Effects on colony Quality – presence of queens and queen egg cells, eggs, larvae and capped brood cell, and food stores (nectar and pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. No TMX-related effects on the Qualitys of the colonies or brood development (comb area with eggs, larvae, capped cells, pollen and nectar cells), egg laying of the queen and the bee brood development were observed (Tables 6-9; Figures 4-7; Appendix 4). Changes in the patterns of increases and decreases were similar between treatments and within the range of normal.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the test item treated crop. There was an apparent transient effect on honeybee mortality; and potentially a transient effect on flight or foraging intensity.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2001k)
Report: Syngenta. 2001. Field Test: Side Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 WS 70 (A 9567 B) on the Honey Bee (Apis mellifera L.) in Spain. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1361 - A9567B. 104 p

The objective of this study was to determine the effects of sunflower (*Helianthus annus*) dressed with TMX as Cruiser® WS 70 (A 9567 B) on the honey bee *Apis mellifera* (Hymenoptera, Apidae) under field conditions following the EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]. A reference chemical (Gaucho – imidacloprid) was used but the data were not included in this assessment. All metrics were compared between the TMX exposed honeybees and the control honeybees on sunflowers. Exposure of honeybees to residues in relevant matrices was evaluated in a companion WoE_{EXP} based on Report CGA2933_1367[34]

Responses 1-10: Quality of methods		Score
Experimental design and hypotheses	The formulated product was Cruiser WS 70; purity of chemical 70%; nominal loading rate of 0.5 kg a.s./100kg seeds; actual loading rate was 0.36921 kg a.s./100 kg seed. Two treatment fields in the south of Spain near Almansa: one (~4 ha) with TMX-treated sunflower (*Helianthus annus* var. Sambro) seeds and one (~4 ha) with TMX-free sunflower seeds (var. Sambro). All seeds were dressed with Quinolate Pro FL (0.25 L/100 kg seeds; Batch 8189; 12 % (w/v) oxine copper and 12 % (w/v) carbendazim), a fungicide which is known to have no insecticidal activity under the test conditions; and each field was sown at a rate of 7.5 kg seeds/ha (Table 2) with a pneumatic 6-line machine. The field sites were located near Almansa (Albacete), Spain, in an area with little agriculture (Table 2, Figures 11-16). No TMX had been used on the fields in previous years. Meteorological data were collected with dataloggers and rain gauge (Table 14, Appendix 1). Six healthy honeybee colonies of similar size and Quality (12 frames for brood and food storage) were placed at the edge of each field on July 23, 1999 at the start of the blooming period (BBCH: 61-62) in two groups of three separated by 30 m; mortality, foraging activity and colony condition were assessed from July 24, 1999 until August 8, 1999. Brood development was assessed from July 24 to September 9, 1999. After flowering (17th of August), all bee hives were transported to a forest area (La Casa Navarro), about 30 km from the test fields in vicinity of the village Teresa de Cofrentes, Spain. The source of the honeybee colonies was provided. Dead bee traps (DBTs) were places at the hive entrance on the hives in the first group of three. Linen sheets (three each 5 $m^{2)}$ were placed in front of the hives in three different places in the field (to cover different stages of flowering, Appendix 10) to record dead bees. The second set of three hives was used for the collection of nectar and pollen from foraging honeybees. Mortality from traps and linens was assessed daily for 16 days starting the day after the hives were placed into the fields. Similarly, for flight intensity, 5 x 1 m^2 were distributed over the fields to encompass different stages of flowering and were assessed three times daily for 16 days starting the day after the	**2**

[34] Syngenta. 2000. Report on Analytical Study 104/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Leafs), Honey, Pollen, and Bee (Honey Stomach Content) Collected in Study 99332/S1-BFEU. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). No. CGA293343_1367 - A9567B. 7 p.

	hives were placed into the fields. Condition of colonies and development of bee brood were checked every 8 (±1) days during flowering starting 1 DAE until four weeks after the end of flowering. The comb area covered by bees, pollen, nectar, eggs, larvae, and capped cells was determined as well as the presence of queen cells and healthy queens. Hive weight changes were determined with a beam scale continuously for two hives in the first group; the weight changes were assessed on July 28, 1999 (DAE 5) and August 2, 1999 (DAE 10) and August 11, 1999 (DAE 19, end of flowering). Honey and pollen were collected from one comb per hive of the second group of three hives during the last three brood assessments. Pollen was also collected from a pollen trap attached to one hive in the second group over a two-day period. The trap was then moved to the second and third hives in the second group over the consecutive two 2-day periods (total of six days). Honeybee behaviour, in front of the hives and in the field, was observed while mortality and foraging observations were made. On the July 28, 30, 31 and August 1, 3, and 6 (DAE 5, 7, 8, 9, 11, and 14, respectively, bees from at least two of the colonies of the second group from each treatment group were caught in front of the hives using a CO_2-gun (LINDE CO_2 snow gun). At least four samples of approximately 200 bees per sample were collected per colony during a 6-day period. The bees were stored at approximately - 20°C in small plastic bags until they were shipped to the lab where the stomachs were processed; the contents were again frozen for possible subsequent analyses for TMX residues. Methods were described in detail p. 21-22. Plant material (leaves and blossoms) and soil samples were also collected as well as dead bees from traps and linens for residue analyses. Dates for activities are provided in Tables 3-5. No statistical procedures were applied to the data (**major weakness**); justification was lamely provided "Statistical analysis was not performed with the mortality data, because every hive is a closed biological system and it is not possible to define the number of bees per hive (population), to which these mortality data belong". No *Nosema apis* spores in bees from each hive were reported (Appendix 7). Results indicated bees were healthy and not influenced by disease.	
Use of GLP and QA/QC.	GLP study with signatures, statement of QA signed. Statement of compliance certificate of authenticity not signed. Deviations and amendments to study plan were provided.	**4**
Exposure concentrations	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). Residue data were provided elsewhere (see above) and TMX residues in nectar (n = 5), and pollen (n = 7) collected by bees were <LOQ of 1 µg/kg; the highest concentration of TMX measured in honey (n = 11) was 1 µg/kg which equates to a dose of 0.3 ng/bee, well below the chronic NOAED of 10.6 ng/bee/day (WoE_{EXP}).	**4**
Transparency of data.	Summary and raw data were included except for behavioural observations. No residue data were included in this report, just the list of samples collected, however residue results are provided elsewhere (see above).	**2**
Number of samples and replication.	There were only two treatments (one TMX and one control), each with 6 hives, pseudo-replication. Repeated measures were made over time. Mortality daily for 16 days; flight intensity three times daily for 16 days; hive weights on three days.	**1**

Overall evaluation of methods		**2.60**
Score for expert judgment on quality of the study- no statistical procedures were applied to the data and no P or r^2 values were provided (**major weakness**).	**0.5**	**1.30**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The average (range) mortality for the exposure phase (Day 1-16) was 8.06 (2.0-18.7) and 2.48 (0-13) dead bees/colony for the TMX and control groups, respectively (Figure 1; Tables 15-16; Appendix 2). The mortality in the TMX treatment group increased in comparison to the control treatment group, but was within the normal range for field studies with honey bees.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The mortality in the TMX treatment though increased relative to that in the control did not result in adverse effects on apical endpoints at the colony level over the study period.	**0**
Mechanism and or mode of action of effect explained	The slight increase in mortality might be due to the higher foraging activity in the TMX treatment group relative to that in the control on DAE 2, 5, 6 and 7 (see Figure 2).	**0**
Overall evaluation of relevance (computed)		
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The average flight intensity was 0.64 and 0.40 bees/m^2 in the TMX treatment group during the entire period (p. 32 and 40, Figure 2; Tables 18-19, Appendix 3), respectively, compared the control treatment group. Negligible differences were observed over the study period. That said on DAEs 4, 5, 6, and 7 of the exposure period, the flight intensity was higher in the TMX treatment (max on DAE 6 of 1.9 bee/m^2) than that in the control treatment (max. on DAE 2 of 1.3 bee/m^2 (Figure 2).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The increased foraging intensity observed during the exposure phase was linked to elevated mortality of honeybees (see above) but the consequence was deemed minimal for apical endpoints at the colony level.	**0**
Mechanism and or mode of action of effect explained	No mechanisms were provided.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee behaviour	**Score**

Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. On all evaluation days, no abnormal behaviour of the bees on the crop and around the colonies was observed compared to the control.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-9. Effects on colony Quality – comb area with bees, brood (eggs, larvae, capped cells) and food stores (nectar & pollen)		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. All metrics were similar between TMX and control treatments and the variability within the normal range (Figures 3-4, 5-6 and Tables 7-8, 9-10); Tables 21-25, Appendix 4).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on colony Quality – hive weights		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. Because of technical challenges only the weights of the second group of hives that were weighed on the days of the brood appraisal were used (Table 13). In the TMX treatment group, the weights of the hives increased during the whole time of the trial. In hive number 2 an increase of 1.3 kg and in hive number 3 an increase of 0.7 kg was measured. In the control treatment group hive number 2 increased (+ 2.2 kg) and hive number 3 decreased (- 0.4 kg).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**

Overall evaluation of relevance (computed)	**0.00**
Overall evaluation of relevance (SEJ).	

Narrative

According to the results it is concluded that the dressing of sunflowers with TMX (A 9567 B) did not cause an intoxication of adult honey bees. Furthermore, there were no effects on the Qualitys of the colonies, condition of the queen and the bee brood development. No residues of TMX in pollen, honey or nectar exceeded the chronic NOAED of 10.6 ng/bee/d for adult or larval life stages of honeybees (see WoE_{EXP}).

Expert Judgement		
QA	Yes	May 17, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2001l)
Report: Syngenta. 2001. Field test: Side Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 350 FS (A-9700 B) on the Honeybee (*Apis mellifera carnica*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1369 - A9700B. 99 p

The objective of this study was to determine the effects of sunflower (*Helianthus annus*) dressed with TMX as Cruiser® 350 FS (A 9700 B) on the honey bee *Apis mellifera carnica* (Hymenoptera, Apidae) under field conditions following the EPPO guideline No. 170[4]. A reference chemical (Gaucho 600 FS – imidacloprid) was used but the data were not included in this assessment. All metrics were compared between the TMX exposed honeybees and the control honeybees on sunflowers. Exposure via residues in matrices (honey from hives, nectar and pollen from honeybees) was evaluated in the WoE_{EXP} based on Report CGA293343_1364-A9567B[35].

Responses 1-10: Quality of methods		Score
Experimental design and hypotheses	The formulated product was Cruiser 350 FS; activity = 35% w/v; nominal loading rate of 42 g a.s./150,000 seeds and the nominal application rate was 18.67 g a.s./ha for TMX treatment. Fungicides were applied concurrently (Table 5). Although there were four treatment fields: one (4.5 ha) with TMX-treated sunflower (*Helianthus annus* var. Alexandra) seeds, one (4.2 ha) reference treatment (Gaucho®) and two (4.5 and 15.0 ha) with TMX-free sunflower seeds (var. Alexandra), only the results for two treatments (TMX and Control 1) are relevant to this assessment. The timing of flowering in Control 1 was similar to that for the TMX treatment. Use of plant protection products applicable to the fields was reported (Tables 2-3). Each field for the TMX and associated control was sown with a SPC-6 drilling machine on April 12, 2000. The field sites were located near Szekszárd, Hungary (p. 14), ~22-30 km from apiary. Meteorological data were collected at the edge of the fields with a digital thermometer, a wind gauge, and an ombrometer vessel (e.g., rain gauge) (Table 16, Figures 6-7; Tables in Appendix 16). Flowering in the field was monitored (Appendix 6); methods were described in detail (Subsection 3.5). The duration of the exposure was 12 days. Fifteen certified healthy honeybee colonies of similar size and Quality (30 combs for brood and food storage) were placed at the edge of each field on June 22, 2000 (DAE 0) when ~70% of crop was in bloom; observations on mortality and foraging activity along a gradient in the field from the hives (100-400 m) were made daily; colony condition was assessed mostly at the beginning and end of the study. Brood size at the start was not specified. After flowering (July 5, 2000; DAE 13), all bee hives were transported back to the apiary in Szekszárd, Hungary. The source of the honeybee colonies was provided. Dead bee traps (DBTs) were placed at the hive entrance of six of the hives.	**3**

[35] Syngenta. 2000. Report on Analytical Study 106/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Flowers), Honey, Nectar, and Pollen Collected in Study 31061/00. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1364 - A9567B. 5 p

	Mortality from traps was assessed daily over the experimental period starting the day after the hives were placed into the fields. For each treatment, foraging, and honeybee behaviour observations were made in the morning daily at the front of 6 of the 15 hives and in the field on four plots (4 x 1 m^2). The number of bees entering the hives was counted for 1 min per colony in the morning on these days as well. Condition of colonies and development of bee brood were checked by the beekeeper at the start and end of the experimental period; brood status was evaluated on 6 of the 15 hives in each treatment. The comb area covered by pollen and nectar was determined for 6 hives at the start and end of the experimental period as well as the comb area covered with eggs, larvae, and capped cells. Methods described were unique. Pollen traps were fitted to 6 colonies and pollen collected from them on two occasions. Hive weight were determined at the start and end of the experiment before transfer to the apiary; methods were not included. Samples of flowers, honey and nectar from two hives and pollen from traps were collected for residue analyses (Table 6). No statistical procedures were applied to the data (***major weakness***); Residue data are presented in another report[36].	
Use of GLP and QA/QC.	GLP study with signatures, statement of QA signed. Statement of compliance certificate of authenticity not signed. Deviations and amendments to study plan were provided. Analytical report included for verification of seed dressing	**4**
Exposure concentrations	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). Residue data were provided in a separate report (see above) and the concentrations of TMX measured in honey from hives and nectar or pollen from honeybees did not exceed the LOQ and were well below the chronic NOAED of 10.6 ng/bee/d.	**4**
Transparency of data.	Summary and raw data were included except for behavioural observations.	**3**
Number of samples and replication.	There were only two treatments (one TMX and one control), each with 6 or 15 hives depending on the endpoint, pseudo-replication. Repeated measures were made over time. Mortality and flight intensity, daily for 11 days and hive weights at start and end of the exposure.	**1**
Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- no statistical procedures were applied to the data **(major weakness)**	**0.5**	**1.50**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. On day 7, there were more than 100 dead bees per colony observed in two of the 6 colonies fitted with DBT in the TMX treatment but this mortality was linked with an insect-control application on one of	**2**

[36] Syngenta. 2000. Report on Analytical Study 106/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Flowers), Honey, Nectar, and Pollen Collected in Study 31061/00. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1364 - A9567B. 5 p

	the adjacent melon fields (p. 34). This was considered a temporary impact that did not affect apical endpoints over the entire study (Tables in Appendix 15). That said, the number of dead worker bees and drones in the TMX treatment was almost twice that for the control treatment (Figure 5) within the first 4 days of exposure.	
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The mortality in the TMX treatment might have resulted in changes to the structure of the colonies in this treatment; however, the change was temporary and did not persist over the entire study period.	**1**
Mechanism and or mode of action of effect explained	No mechanism other than change in hive structure was proposed.	**0**
Overall evaluation of relevance (computed)		**1**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee foraging activity – # bees entering a hive; # on flower heads;		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The summarized results are shown in Table 7 and Figure 3; the detailed data are given in Appendix 7. In the TMX treatment; the average number of bees on the sunflower heads for the TMX hives was 55.2 bees per 400 flowers/d and 19.4 and 94.7 bees/400 flowers/d for the other two control treatments (Table 7, Figure 3). The average number of bees entering the hives in the TMX and control treatments was 25.5 and 22.8-30.3 bee/colony/minute (Table 8, Figure 4); however, the number of bees returning with orange-red pollen loads was 5.4 and 3.7-11.9 bee/colony/minute, respectively.	**1**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The lower number of foraging bees on the sunflowers and the lower number of bees returning to the hives with sunflower pollen loads suggests that a significant amount of both nectar and pollen collected in these colonies was not from the seed-treated sunflowers but from other off field-plants as the area of pollen stored within all hive increased in a similar manner.	**1**
Mechanism and or mode of action of effect explained	No mechanisms were proposed.	**0**
Overall evaluation of relevance (computed)		**0.67**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. No abnormal behaviour of the bees was observed during foraging and around the hives (subsection 4.1).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**

reproduction, and fitness)		
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-7. Effects on colony Quality – brood size, comb area with brood (eggs, larvae, capped cells)		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The number of inhabited combs of hives in the TMX field decreased by 2.6%, while it increased by 2.9% in control 1 and by 1.6% in control 2 (Table 10 and Appendix 10). The average number of combs with brood decreased in all fields (Table 11 and Appendix 11). Comb areas for capped brood decreased by 28.2-31.7% for all fields. The comb area with larvae increased by 42.6%in the TMX and decreased by 5% in control 1. The comb area with eggs increased in all fields by 18.3-36.5% (Table 12 and Appendix 12). The significance of these changes is difficult to discern.	**2**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The significance in the change in brood structure between treatments cannot be addressed without statistical analyses of the data; however, the conclusion in the study was that it was of little consequence (e.g., "Under the conditions of this experiment the TMX as a Cruiser 350 FS (A-9700 B) seed-dressing product used at a dose of 0.120 L product/150,000 sunflower seeds and a sowing rate of 66,667 seeds/ha was not harmful to the bees or the bee colonies, the nectar collection was not affected"). This conclusion is questionable under the circumstances.	**1**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**1.00**
Overall evaluation of relevance (SEJ).		

Response 8-9. Effects on colony Quality – nectar & pollen storage		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. During the experiment the area of the combs containing stored pollen increased on average in all the fields. The average and summarized results are shown in Table 13, and the detailed data are provided in Appendix 13. The area of the combs containing stored honey (Table 14) decreased to a similar extent throughout the experiment in the TMX-treated field (on average 19.9 %) and in the Control #1 field (on average 20.9 %) (Appendix 14).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Because the losses occurred in both the TMX and Control #1 treatments, a conclusion was drawn that there was no significant difference between treatments. The conclusion was that this decrease was not related to TMX.	**0**

Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on colony Quality –hive weights		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. Hive weights decreased in the TMX treatment by 2.9% and increased in the control treatments by 5.7 and 14.5% respectively (p. 25). Table 9 shows a weight decrease of 1.1 kg for TMX and an average weight gain of 2.1 kg for the control 1 hives. The hive weight gain for the second control was 5.6 kg. The variability is within the normal range (Table 9 and Appendix 9). A weight gain is expected for all colonies.	**2**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	There is no way of gauging the significance of this difference. However, it cannot be ignored and the data require quantitative and statistical analyses to determine if these observed and reported differences are relevant. The assumption is that hive weight is an apical endpoint and there was an impact.	**2**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**2**
Overall evaluation of relevance (computed)		**2.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	May 17, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2001m)
Report: Syngenta. 2001. Field test: Side Effects of Sunflowers Grown from Seeds Dressed with CGA 293343 350 FS (A-9700 B) on the Honeybee (*Apis mellifera carnica*). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1370 - A9700B. 77 p

The objective of this study was to determine the effects of sunflower (*Helianthus annus*) dressed with TMX as Cruiser® 350 FS (A 9700 B) on the honey bee *Apis mellifera carnica* (Hymenoptera, Apidae) under field conditions. All metrics were compared between the TMX exposed honeybees and the control honeybees on sunflowers. The residue results are summarized in the WoE_{EXP} and in Report CGA293343_1365[37].

Responses 1-10: Quality of methods		Score
Experimental design and hypotheses	The TMX-treated field of 63.2 ha and the control field of 155.0 ha were in the vicinity of Tolna (Szekszárd), Hungary. In both fields, sunflower seeds (TMX treated and TMX-free or untreated) (var. Alexandra) were sown at a rate of 63,200 seeds/ha. The type of soil was calcareous humus alluvial soil in the case of the TMX-treated field and calcareous chernozem for the control field. The sowing conditions, the plant growth and the other plant protection product treatments were the same in both fields. The flower development occurred concurrently in both treatments (Subsection 3.4.4). The formulated product was Cruiser 350 FS; activity = 35% w/v; nominal loading rate of 42 g a.s./150,000 seeds and the nominal application rate was 17.696 g a.s./ha for TMX treatment. Use of plant protection products applicable to the fields was reported (Tables 2-3) including use of fungicides on the seeds (Table 5). Each field for the TMX and control was sown on April 12, 2000 and April 11-13, 2000, respectively, and two IHC-Cyclo-400 seeder machines were used. The field sites (TMX and Control) were located near Szekszárd, Hungary (p. 14), ~26-28 or 22-24 km, respectively, from the apiary (Appendix 1). Meteorological data were collected at the edge of the fields with a digital thermometer, a wind gauge, and an ombrometer vessel (Table 16, Figures 6-7; Tables in Appendix 13). Flowering in the field was monitored (Appendix 4); methods were described in detail (Subsection 3.4 and 3.5). The fields were surrounded by other crops but none flowering at the same time as sunflower. The duration of the exposure was 12 days. Fifteen certified healthy honeybee colonies of similar size and Quality (30 combs for brood and food storage) were placed at the edge of each field in the evening of June 22, 2000 (DAE 0) at the start of flowering; observations on mortality and foraging activity along a gradient in the field from the hives (100-400 m) were made daily; colony condition was assessed mostly at the beginning and end of the study. Brood size at the start was not specified. After flowering (July 4, 2000; DAE 12), all bee hives were transported to the apiary in Szekszárd, Hungary. The source of the honeybee colonies was provided. Dead bee traps (DBTs) were placed at the hive entrance of six of the hives.	**3**

[37] Syngenta. 2000. Report on Analytical Study 107/00 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sun Flower (Heads and Flowers), Honey, Nectar, and Pollen Collected in Study 31062/00. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1365 - A9567B. 5 p

	There were 20 other bee colonies placed near the TMX-treated field from a different apiary during the study. Mortality from traps was assessed daily over the experimental period starting the day after the hives were placed into the fields (June 24 to July 3, 2000). For each treatment, foraging and honeybee behaviour observations were made daily in the morning, at the front of 6 of the 15 hives and in the field on four plots (4 x 1 m^2). The number of bees entering the hives was counted for 1 min per colony in the morning on these days as well. Condition of colonies and development of bee brood were checked by the beekeeper at the start and end of the experimental period; brood status was evaluated on 6 of the 15 hives in each treatment. The comb area covered by pollen and nectar was determined for 6 hives at the start and end of the experimental period as well as the comb area covered with eggs, larvae, and capped cells. Methods described were unique. Pollen traps were fitted to two colonies and pollen collected from them on two occasions. Hive weights were determined at the start and end of the experiment before transfer to the apiary; methods were not included. Samples of flowers, honey and nectar from two hives, and pollen from traps were collected for residue analyses (Table 6). Residue data are presented in another report[37] No statistical procedures were applied to the data (***major weakness***).	
Use of GLP and QA/QC.	This was GLP study but was conducted in consideration of the GLP principles outlined The OECD Principles of Good Laboratory Practice in the Testing of Chemicals ENVIMC/CHEM(98) 17 and GLP regulation of Hungary 31/1999. (VIII.6.) EUM-FVM. QA statement and audits were completed.	**4**
Exposure concentrations	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included; however, they were available as cited above. The concentrations of TMX measured in honey collected from hives and nectar and pollen collected by honeybees exposed to TMX via sunflowers grown from seeds dressed with TMX were less than the chronic NOAED for honeybees of 8.6 ng/bee/d.	**4**
Transparency of data.	Summary and raw data were included except for behavioural observations.	**3**
Number of samples and replication.	There were only two treatments (one TMX and one control), each with 15 or 6 hives depending on the endpoint; regardless, the hives were not independent replicates (i.e., pseudo-replication). Repeated measures were made over time. Mortality daily for ten days; flight intensity daily for ten days; hive weights at the start and end of the exposure.	**1**
Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- no statistical procedures were applied to the data (***major weakness***)	**0.5**	**1.50**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The mortality of bees was similar between treatments for the field assessments (Figure 5) and was below 100 bees per colony per	**0**

	day which is an acceptable level of natural mortality for bees in this region (Subsection 4.6) The average results are shown in Table 15 and Figure 5 with supporting data in Appendix 12.	
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	No mechanism other than change in hive structure was proposed.	**0**
Overall evaluation of relevance (computed)		**0.0**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee foraging activity – # bees entering a hive; # on flower heads;		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The summarized results for # bees on flower heads are shown in Table 7 and Figure 3; the detailed data are given in Appendix 5. Daily observations resulted in an average of 25.0 foragers on 100 sunflower heads in the TMX-treated field and 22.6 foragers on sunflowers in the control field. The average number of bees entering the hives in the TMX and control treatments was 32.6 and 22.9 bee/colony/minute (Table 8, Figure 4, details in Appendix 6); however, the number of bees returning with orange-red pollen loads was 13.8 and 4.3 bee/colony/minute, respectively.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.0**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. No abnormal behaviour of the bees was observed during foraging and around the hives (subsection 4.1).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**

Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-7. Effects on colony Quality – brood size, comb area with brood (eggs, larvae, capped cells)		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. During the experiment the number of the inhabited combs increased by 12.7% in the TMX-treated field and by 12.4 % in the control field (Table 10 and Appendix 8). The average number of combs with brood remained the same within treatments (Table 11 and Appendix 9). Comb areas for capped brood and eggs decreased in hives in both treatments and was similar between treatments; however, the comb area with larvae increased by 10.1% in the TMX-treated field whereas it decreased by the same amount (10.8%) in hives from the control field (Table 12; Appendix 10). The brood development and structure was otherwise similar in both treatments and within the variability that would be expected.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8-9. Effects on colony Quality – honey & pollen storage		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. During the experiment, the area of the combs containing stored pollen increased on average in all the fields. The average and summarized results are shown in Table 13, and the detailed data are provided in Appendix 11. The area of the combs containing stored honey (Table 14) increased to a similar extent throughout the experiment in both treatments (52.7% and 30.9 % for the TMX and control treatments, respectively). The increase in pollen storage was 67.3% and 35.2%, respectively, for TMX and control treatments.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The flowering period was relatively short but the weather conducive to foraging. The honey yield was lower than expected in both treatments.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on colony Quality –hive weights		Score
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. Hive weights increased in both the TMX treatment and the control treatments by 17.0% (6.6 kg) and 15.8% (6.0 kg) respectively (p. 23 and 26; Table 9; Appendix 7). A weight gain is expected for all colonies.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative:
The number of flower visits on the sunflower heads was about 10 % greater in the treated field compared to the control field. The average number of the bees returning to the hives was 42% more in the TMX-treated field than in the control field. The increase in the area of the combs containing stored pollen during the experiment was 2.8-times more and the area of stored honey was more than 2- times more in the TMX-treated field than in the control field. It was most likely to have been influenced by the fact that the fading of the flowers started earlier on the control field.

Under the conditions of this experiment the TMX seed dressing used at a dressing rate of 0.12 L product/150,000 sunflower seeds and sown at a rate of 63,200 seeds/ha was not harmful to the bees or the bee colonies and the nectar collection was unaffected.

Expert Judgement		
QA	Yes	May 18, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2001n)
Report: Syngenta. 2001. Semi-Field Test (Tunnel): Side Effects of Sunflower Grown from Seeds Dressed with A-9567 B on the Honey Bee (*Apis mellifera*) in Spain. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1375 - A9567B. 65 p

A semi-field (tunnel) GLP study was conducted to investigate the effects on honeybees (*Apis mellifera* L.) of TMX (Cruiser 70 WS) applied as a seed dressing to sunflowers (*Helianthus annus)* near Ayora in the province of Valencia, Spain (Figure 1).

Responses 1-6: Quality of methods		**Score**
Experimental design and hypotheses	The objective of this study was to determine the side effects of sunflower, dressed with TMX, on honey bee *Apis mellifera mellifera* L in comparison to untreated sunflower under semi-field conditions (tunnel tunnels) following EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]: Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Point 5.3. The test product a.s. was verified to be 69.7% and the seeds were dressed concurrently with a fungicide (Apron XL 350 ES – 200g metalaxyl-M/100 kg seed). The loading rate was measured to be 339.9 g a.s./100 kg seed and the seed dressing procedure was described. The TMX-free seeds in the control treatment were the same variety and treated only with the fungicide. Soils were characterized (Table 2). Meteorological data were recorded with data loggers and flower development monitored daily (Table 10 in Appendix A1). There was one site divided into two treatment plots (~15 x 150 m) in which one plot was sown at 7.45 kg seed/ha with TMX-treated (0.5 kg TMX/100 kg seeds) sunflower seeds (var. Carlos) and on plot was sown at 7.4 kg seeds/ha with TMX-free seeds. Three tunnels/tents (150 m^2) were established on each treatment and one honeybee hive (healthy even Quality – 6 combs with ~10,000 bees) was placed into each tunnel. Criteria for hives included at least two brood combs containing eggs and at least one honey and pollen comb and the hives were deemed to be healthy. Hives were introduced to the tunnels at the start of full bloom (BBCH 63) on July 10, 2000 and three days were allowed for acclimation. The hives were equipped with dead bee traps at the entrance (Appendix A3). Linen sheets (~40 m^2) were also placed into each tunnel to assess honeybee mortality (Figure 2 and 6). Measurement endpoints included honeybee mortality, foraging activity and honeybee behaviour which were assessed daily for 7 days (July 13-19, 2000; Tables 4, 5, and 7) and colony condition which was assessed 2 days before the hives were set up on July 10, 2000, and at the end of the exposure period (July 8, 2000 and July 20, 2000) (p. 11; Tables 6 and 7). Flight in intensity was assessed 3 times/d for 7 days. Samples of plant material and dead bees were collected during the study for residue analyses; however, no residue data were included in this study. Statistical procedures were applied to the mortality data (SAS release V8) but not to the data for other apical endpoints (***major weakness***);	**2**

	assumptions were tests and procedures describe and a 95% probability was used (p = 0.05).	
Use of GLP and QA/QC.	GLP study; certificate of quality assurance was included and audit dates provided; study plan deviations were reported and amendments included.	**4**
Exposure concentrations	Only one application rate was applied and was verified. No residue data for bee-relevant matrices were reported but, as this was a tunnel study with verified treatments, this in a *potential weakness*	**1**
Transparency of data.	Summary data and raw data were included except for honeybee behaviour.	**3**
Number of samples and replication.	Two treatments each with 3 non-independent tunnels, each with one hive (no independent replication, only pseudoreplication); repeated measures were made on consecutive days (n = 7) or at the beginning and end of the study (n = 2).	**2**
Overall evaluation of methods		**2.40**
Score for expert judgment on quality of the study- statistical procedures were applied to only one endpoint (**major weakness**)	**0.5**	**1.20**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	The mean mortality (dead bees in the bee traps and on the linen sheets per day) in the TMX treatment was significantly higher only on DAE + 3 (18.7 dead bees/day) in comparison to the control group (8.0 dead bees/day) (Dunnett U -test; p = 0.05). On other assessment days, there were no significant differences between treatments (Figure 3; Tables 14 and 15, Appendix A2). The mean mortality over the entire observation period was 9.9 dead bees per tunnel per day in the TMX treatment group and 11.8 dead bees per tunnel per day in the control group.	**4**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Because the effect only occurred on one of seven days, it was concluded that there was no persistent impact on mortality.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**1.33**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values provided. The mean number of foraging and flying bees per day ranged from 35.4 to 71.6 bees/25 sunflowers in the control and from 32. 1 to 67.1 bees/25 sunflowers in the TMX treatment group (see Table 16 - Table 17 in the Appendix A2). The mean flight intensity observed over the entire observation period was 49.9 bees on 25 sunflowers in the TMX treatment group and 52.2 bees on 25 sunflowers in the control group (Figure 4). Flight intensity was similar between treatments.	**0**

Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on colony Quality – honeybee behaviour		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r2 values provided. The bees visiting the sunflower dressed with TMX showed normal and intensive pollen and nectar collection with no differences from that observed for the control treatment group. On all evaluation days, no abnormal behaviour of the bees on the crop and around the colonies in the TMX treatment were observed compared to the control.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-6. Effects on colony Quality – brood development (eggs, larvae, pupae)		**Score**
Statistical significance of responses	No statistical analyses of data were conducted and no P or r2 values provided. During the observation period, changes and fluctuations in the relative amount of the different brood stages, i.e. egg stage, larval and pupal stages, occurred in almost every colony of the test item (Table 9) and control group (Table 8). No TMX- related effects on brood development were observed (Table 18-19, Appendix A2).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative
There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the test item treated crop.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2001a)
Report: Syngenta. 2001. Field Test: Effects of Oil-Seed Spring-Rape Grown from Seeds Dressed with CGA 293343 WS 70 (A 9567 B) on the Honey Bee (*Apis mellifera* L.) (Conducted in Southern Germany near Pforzheim). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1376 - A9567B. 95 p

The field study was carried out according the EPPO guideline No. 170[29] and the SETAC guideline (1995)[32] to assess the effects of TMX-treated spring oilseed rape (sOSR) on honeybees (*A. mellifera*). The objective of the study was to determine the effects of sOSR dressed with TMX on the honey bee *Apis mellifera* (Hymenoptera, Apidae) under field conditions. This study is similar to that describe for the one conducted in northern Germany[38] and similar to the study conducted in this area using wOSR[39].

Responses 1-10: Quality of methods		Score
Experimental design and hypotheses	There were two fields in which TMX-treated and TMX-free (*Brassica napus* var. Licosmos) sOSR seed were sown with an Accord Pneumatic machine. The seeds in the TMX treatment were dressed with Cruiser WS 70 at a loading rate of 0.6 kg test product/100 kg seed (nominal 0.4206 kg a.s./100 kg seed; confirmed 0.4322 kg a.s./100 kg seed) and sown at a rate of 7.0 kg seed/ha; the size of the TMX-treated field was 2.1 ha. The control field was 2.1 ha and sown on April 1, 1999 but again on May 4, 1999 with seed that had been dressed with Isofenphos (insecticide) and TMTD (thiram -fungicide) but were TMX free. The second sowing was at 7.50 kg/ha (Table 2) and necessary because of insect damage. Loading rates were confirmed and a certificate of analysis provided (Appendix 10). The fungicide and insecticide added to the control seed is a *potential weakness* because these were not added to the TMX-treated seed. The fields were in southern Germany near Pforzheim and were separated by a distance of 4.2 km (Figures 11-14). Flower development was monitored (Appendix 5). Meteorological data were collected at a weather station ~10 km from the sites. Assessment dates and activities are provided (Table 3-6) Six certified-healthy, queen-right honeybee colonies of similar size and Quality (each with ~30,000 bees/hive) were placed near the TMX-treated field prior to full flowering of sOSR on June 13, 1999 and June 28, 1999 near the control field. The time difference accommodated the flower development in that both groups of hives were in the field when the sOSR was at 30% flower (BBCH: 63-64). Each hive comprised 1-2 brood bodies with 6-8 brood frames and one honey body with at least 8 frames. The hives were placed in the respective treatment fields in two groups of three. Three hives in the first group were equipped with dead bee traps (DBTs) at the entrance. Linen sheets were also placed in the field and at the hive entrance and in the field (3 x 5 m^2) used to monitor	**2**

[38] Syngenta. 2001. Field Test: Effects of Oil-Seed Spring-Rape Grown from Seeds Dressed with CGA 293343 WS 70 (A 9567 B) on the Honey Bee (*Apis mellifera* L.) (Conducted in Northern Germany near Celle). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1360 - A9567B (99125/02-BFEU). 98 p
[39] Syngenta. 2001. Field Test: Side Effects of Oil-Seed Winter-Rape Grown from Seeds Dressed with Cruiser OSR (A9807 C) on the Honey Bee (*Apis mellifera* L.). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA173506_5423 - A9807C (99393/01-BFEU). 80 p

	honeybee mortality (Appendix 9). The second group of hives was located at 30 m from the first group and were used primarily for the collection of honey stomachs of foraging bees and the pollen. The number of dead bees found in front of the hives on the linen sheet and in the dead bee traps was recorded and the dead bees were removed once a day, in the morning, during a period of either 9 and 8 days for the TMX and control treatments, respectively starting 2 and 3 days (resp.) after the hives were introduced. Foraging activity and flight intensity were measured three times per day in 5 assessment plots of 1 m^2 starting one day after setup for a period of either 9 or 10 d. Honeybee behaviour was evaluated during the assessment period in front of the hive and in the field. Starting one day after set until the end of flowering, colony condition and brood status were evaluated every 8 days (±1). The last check of control colonies was either 23 or 34 d after the end of flowering (August 6 and 17, 1999); the last check of the TMX colonies was 30 d after flowering (July 24, 1999) (Tables 3-6). Hive weights were measured at specific time periods during brood appraisal and one hive in each treatment (Group 1) was on a beam scale and weights were recorded continuously. Methods cited included EPPO guideline No. 170[4] and the SETAC guideline (1995)[32]. The hives were removed from the test sites on June 24 and July 14, 1999, for TMX and control colonies, respectively, and returned to the apiary (garden in Niefern-Öschelbronn, Germany) for monitoring; therefore, the duration of exposure was 11 and 16 d, respectively and the last brood assessments were done on July 24, August 6, and August 17, 1999 on days 41, 39 and 50 after the first day of exposure for TMX, C5 and C6, and C1-C4, respectively (Tables 3-6). Methods for biological data collected were described in detail in Subsection 4.5 and summarized in Tables 3-6. Endpoints measured included mortality; flight intensity/foraging activity, and condition of the colonies; colony Quality (# of combs covered by bees and brood); the presence of health queens (eggs & queen cells); the comb area with food storage (pollen & nectar); pollen from pollen traps; and brood development (comb area with eggs, larvae, and capped cells). Hive weight was measured daily on one colony in the first of group of three hives for each treatment using a beam-scale. Weights were recorded at night when the bees were in the hive. Honeybee behaviour in front of the hive and in the field, was observed. No statistical procedures were applied to the data; comparisons were made between the endpoint metrics in the TMX group with those for the control group (**major weakness**). No P values or r^2 values were reported. Samples of honeybees, plant material (leaves and flowers), contents from foraging honeybee stomachs, nectar and honey from the hives were collected for residue analyses which was not reported in this study. No residue data were included in this report (*weakness*).	
Use of GLP and QA/QC.	The study followed GLP and included a statement of compliance, statement of quality assurance with proof of audits, study plan, deviations from study plan and plan amendments and was conducted by a GLP certified testing facility.	**4**
Exposure concentrations	There were two treatments each with one field and 6 hives each, which were sampled in two groups of three. Although samples were collected for residue analyses; no residue data were reported.	**0**

Transparency of data.	Summary and raw data were included; no behaviour data were included		**3**
Number of samples and replication.	Samples and observations were made for each endpoint over time (repeated measures) but there were no true (independent) replicates; hives were pseudo-replicates.		**1**
Overall evaluation of methods			**2.00**
Score for expert judgment on quality of the study- no statistical analysis of data is a **major weakness**		**0.5**	**1.00**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values provided. During the evaluation period, daily mortalities ranged from 2.0 to 11.3 and from 1.0 to 6.3 dead bees/hive for the TMX and the control treatments, respectively (Figures 1 & 2; Tables 17 &18). The average mortality was 4.8 and 3.9 dead bees/colony, respectively. Treatment comparisons were deemed impossible because the assessments were not done concurrently (**we disagree**). The average mortality between treatments is similar and within the normal range.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.0**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity/foraging activity		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P values or r^2 values reported. Immediately after the start of exposure (1 and 2 DAE), the flight intensity of bees in the TMX treatment was twice that of the control bees (Figures 3 & 4; Tables 19 & 20); however, by day 3, the acute difference was no longer there. Over the entire exposure period, the average flight intensity was 5.7 bees/m^2 in the TMX treatment and 6.1 bees/m^2 in the control treatment. Flight intensity was essentially similar for the two treatments.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**

Overall evaluation of relevance (computed)	**0.0**
Overall evaluation of relevance (SEJ).	

Response 3-8. Effects on colony Quality – presence of queens and queen egg cells, eggs, larvae, capped brood cells, and food stores (nectar & pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P values or r^2 values reported. The six colonies comprising the TMX treatment, developed normally in terms of Quality and brood. The colony Quality and brood development of the first group of three hives in each treatment were similar (Figures 5 & 7; Tables 7 & 9). The continued presence of eggs showed that the queens were in good condition in all colonies of the TMX treatment. A comparison of the second group of three hives in each treatment, showed a similar result (Figures 6 & 8; Tables 8 & 10). Also in the last colony check by the beekeeper prior to winter no differences were observed between the colonies of the test item and the control treatment. There were no differences in food stores between treatments.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 9. Effects on colony Quality – hive weight		**Score**
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. Hive fluctuations were relatively small for colonies in the TMX treatment; there was no sustained weight gain. In the control hives, there was a gradual weight gain over the first 6 days and hive weights, thereafter, were relatively unchanged (Tables 11 and 12). These data are challenging to interpret without statistical analyses of the data.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.0**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on honeybee behaviours		Score
Statistical significance of responses	No statistical procedures were applied to these data and no P or r^2 values reported. There were no significant differences in honeybee behavior for the two treatments (Subsection 7.5); no abnormal behaviour was reported.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA). No residue data were included.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the test item treated crop. There was an apparent transient effect on honeybee mortality; effects on flight or foraging intensity were also transient.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 5, 2016

(Syngenta 2001f)
Report: Syngenta. 2001. Field Test: Side Effects of Sunflower Grown from Seeds Dressed with A-9567 B on the Honey Bee (*Apis mellifera* L.) in Italy. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1391 - A9567B. 94 p

This report describes the effects of TMX-treated sunflowers (*Helianthus annus*; var. Carlos) on honeybees in a field study conducted in Italy according the EPPO guideline No. 170[29] and the SETAC guideline (1995)[32]. The analysis of samples of flower-heads, leaves, honey, pollen and nectar collected by bees from sunflowers exposed via seed-dressing with TMX is presented in the WoE_{EXP}[40]. Imidacloprid was used as reference but is not discussed in this WoE.

Responses 1-12: Quality of methods		Score
Experimental design and hypotheses	This was a field-study conducted near Bologna in Italy. There were three treatment fields, a TMX-treated, a control, and a reference. All fields were approximately 2 ha in size and the test item to control and reference fields were ~20 km apart, however the reference and control fields were only 4 km apart. No imidacloprid had been used in the fields in the last few years. Sunflower seeds (var. Carlos) were treated with TMX as Cruiser® 70 WS (A-9567 B). Application rate on seeds was measured at 339.9 g a.s./100 kg seeds. All seeds were treated with the fungicide Apron XL 350 ES (200 g a.s. metataxyl-M/100 kg sees); use of other pesticides on the sunflowers during growth was not reported. A reference field was treated with imidacloprid (imidacloprid as Gaucho 70 WS). Seeds were sown (Table 2) with an Agricola Italiana Massanzago PD pneumatic seeder on April 17, 2000 at a rate of 88,949 seeds/ha for the test item field and 97,544 seeds/ha for the control field. Meteorological conditions were recorded during the study and combined with data from local weather stations (Tables 11 - 16). Assessment dates were provided (Tables 3-6) Eighteen hives were used in the study, six in each of the TMX, reference, and control fields. Honeybees (*Apis mellifera ligustica*) were from a local commercial source and certified as healthy. Each hive contained 1 brood body with at least 5–9 brood frames and 1–2 honey body with 8–10 frames. Number of bees per hive was 25,000–35,000. The hives were placed either in or near the fields when the sunflowers were at BBCH-stage: 59-62, start of blooming (June 21, 2000) in two groups. After flowering (July 1, 2000), all bee hives were transported to another location (near Molinella, Italy, Figure 7, Appendix A1). Three of the six hives were equipped with dead bee traps (DBTs) and were located at the edge of the fields. Additionally, three linen sheets (each 5 m^2) were placed at three different locations in the field (Appendix 8) and one in front of the hive to monitor mortality. The remaining 3 hives in each field were positioned at least 30 m away from the first set of 3 hives and the latter was used for the collection of honey and pollen from foraging bees. Observations on flight intensity were made in five assessment areas (Figure 8-10, Appendix A1) each with 25 sunflower plants over an 8-d period. Brood development assessments were made	**3**

[40] Syngenta. 2001. Report on Analytical Study 103/01 Determination of Analytes Thiamethoxam (CGA 293343) and CGA 322704 in Sunflowers (Flowers, Leaves), Honey, Honey Stomach Content, and Pollen, Collected in Study 20001072/I1-BFEU. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1411- A9567B. 5 p

	every 8±1 d during the flowering period. The first assessment occurred at the start of exposure and the last four weeks after the end of the flowering period. Quality of colony was reflected by the comb area with bees, pollen and nectar, as well as, the presence of a health queen (eggs and queen cells) and brood development was reflected by the comb area with eggs, larvae and capped cells. Assessment methods were described. Hive weights were recorded continuously with a beam scale and daily weights recorded when bees were in the hive from June 23 (DAE 2) to July 2, 2000 (DAE 11). Honeybee behavior was assessed daily for 8 d in front of the hive and in the field. Statistical procedures were applied to only the mortality data (***major weakness***) and assumptions were tested; procedures were described or cited. Significance was specified as $p \leq 0.05$ (Subsection 4.8.1). Endpoint measurements included honeybee mortality from DBTs, foraging activity (intensity), hive weights, colony Quality and brood development. The bees in the DBTs and on the linens, were removed daily for a period of eight days. Sampling of honey took place on August 8, 2000 from the first group of hives (Group 1) and during the hive appraisals for the second group (Group-2) on June 23 and 30, 2000. Honey was extracted from the comb with a honey extractor or the entire honey comb was removed and placed into a plastic bag. All samples were stored at -18C. Pollen traps were used to collect pollen from returning foragers. Nectar was collected from the honey stomach. Forager bees were collected four times per colony with a CO_2 gun and were stored at -18C and shipped at the same temperature to the Niedersächsisches Landesinstitut für Bienenkunde for removal of the nectar from the honey stomach. Methods are described in the report and summarized in the WoE_{EXP}. Samples of flower heads and leaves were taken for analysis and only leaves contained detectable residues of TMX only. Analyses of samples used LC MS/MS. Analyses followed standard methods. Isotopically labeled internal standards were not used but standards of purity >99% were used to develop standard curves. The LOQ was 1 µg/kg and recovery of TMX from honey and pollen ranged from 95–102% and 83-84% respectively. Recovery for clothianidin was 101–110% and 78–87% respectively. TMX was detected in pollen collected from the control hives (1.1 µg/kg) (*weakness*).	
Use of GLP and QA/QC.	The effects component and the analysis of residues were conducted under GLP with QA. Weather data were not recorded under GLP. Deviations from and amendments to the study plan were provided.	**4**
Exposure concentrations	There was only one application rate of TMX; the highest residue concentration measured in pollen collected by honeybees and from flowers (n = 3) was 3.2 µg/kg which corresponded to a calculated dose of 0.4 ng/bee which is well below the chronic NOAED of 10.6 ng/bee/d (WoE_{EXP}). Residues in honey (n = 6) from the hive were less than the detection limits.	**4**
Transparency of data.	Summary and raw data were provided, except for behavioural observations.	**3**
Number of samples and replication.	There was only one site per treatment but there were six pseudo-replicated hives per site, which were sampled in groups of three.	**1**

Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- Statistical procedures were not applied consistently to all endpoints only to the mortality data (***major weakness***)	**0.5**	**1.50**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	There were no significant differences (P>0.05; Table 7) for the number of dead bees in the DBTs between the TMX and control treatments from DAE 3 to 6. On day 7 after the start of bee exposure, the number of dead bees in the DBTs increased in the TMX treatment group (55.3 dead bees/colony) in comparison to that for the control (3.67 dead bees/colony) (Figure 1, Table 7). The average daily mortality during the evaluation days DAE 3 - 10 was 16.9 dead bees/colony for the TMX treatment group which was slightly higher than that for the control group (15.3 dead bees/colony for the control group) (Tables 21-23, Appendix A2). The number of dead bees found on the linen sheets was 0.1 and 0 dead bees/day for treatment and control, respectively, which constitutes minimal mortality.	**4**
Concentration- or dose-response	There was only one application rate of TMX and a control field each with 6 hives; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Significantly higher numbers of dead bees were recorded in the TMX treatment group relative to that in the control group on days 7, 8 and 10 but not on day 9. There were no apparent persistent consequences attributed to the higher mortality in the TMX treatment.	**1**
Mechanism and or mode of action of effect explained	No mechanism was proposed as the effect of increased mortality was not corroborated by effects on other endpoints.	**0**
Overall evaluation of relevance (computed)		**1.67**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	There were marginal differences in flight intensity over the crop between the control and TMX treatment groups. The flight intensity in the TMX group over the entire period of observation was 12.1 forager bees/25 sunflowers compared to 9.4 forager bees/25 sunflowers in the control treatment (Figure 2; Tables 24-26, Appendix A2). Flight intensity was similar to that for the control group; variability was high.	**0**
Concentration- or dose-response	There was only one application rate of TMX and a control field each with 6 hives; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on colony Quality – hive weights		Score
Statistical significance of responses	The changes in hive weights over the study were comparable among treatments (Tables 8 and 10). The weight increase was between 8.1 and 12.9 kg in the TMX treatment and 7.2 and 14.8 kg per colony in the control and the pattern of increase was similar.	**0**
Concentration- or dose-response	There was only one application rate of TMX and a control field each with 6 hives; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-11. Effects on colony Quality - brood development (brood nest size, comb area with eggs, larvae, capped cells, honey, pollen), presence of healthy queen & queen cells		Score
Statistical significance of responses	Brood development was variable among hives within and between treatments (Figures 3 and 5; Table 27, 28, 31, 32, Appendix A2). At the end of the study, there were no significant differences between the TMX and the control hives for eggs were present, queens healthy, and colonies in good condition.	**0**
Concentration- or dose-response	There was only one application rate of TMX and a control field each with 6 hives; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 12. Effects on honeybee behaviour		Score
Statistical significance of responses	On all evaluation days, no abnormal behaviour of the bees on the crop and around the colonies was observed in the test item compared to the control.	**0**
Concentration- or dose-response	There was only one application rate of TMX and a control field each with 6 hives; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**

Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative
There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the test item treated crop.

Expert Judgement		
QA	Yes	May 18, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2001e)
Report: Syngenta. 2001. Semi-Field Test: Side Effects of Oil-Seed Spring-Rape (*Brassica napus*) Dressed with Different Rates of CGA 293343 on the Honey Bee (*Apis mellifera* L.). Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1833 - A9807C, A9567C. 103 p

The aim of this study was to investigate possible side-effects of dressing of spring oilseed rape (sOSR) seed with TMX on honey bees under semi-field conditions (tunnel) in southern Germany. The seeds were dressed with the maximum application rate of TMX (1x) as well as five higher application rates representing overdressed rates of 2x, 3x, 4x, 6x and 8x.

Responses 1-8: Quality of methods		**Score**
Experimental design and hypotheses	Seeds of *Brassica napus* (var. Forte) were sown at a nominal rate of 8 kg/ha with an Accord pneumatic driller on May 26, 2000 on 8 plots that were 6x15 m near Pforzheim, in the region of Baden-Württemberg, Germany at Katharinentaler Hof (Figure 3, Tables 1 & 4). Two plots served as controls and there were six treatment plots representing 1x, 2x, 3x, 4x, 6x, and 8x the application rate (AR) of 420 g a.s. TMX/100 kg seed (Figure 1). The confirmed rates of measured concentrations: 429.0, 814.1, 1265.4, 1686.3, 2487.4 and 3303.6 g a.s. TMX/100kg seeds (p. 11 and Table 3). One control plot was planted with un-treated sOSR (C1) and the other plot (C2) sown with seeds treated with a fungicide CGA 329351. One tunnel was established on each plot and the control plots were separated from the treatment plots by 5 m. Within each tunnel, linen sheets (Figure 2) were laid in 0.6 m strips along the front side of the tunnel walls and through the middle of the plots leaving each side (4.4 x 2.2 m) covered with sOSR. Meteorological data were provided (Table 10, Appendix A2). Flowering was assessed and data provided (Table 12, Appendix A2). Statistical procedures were applied to the flight intensity data only (***major weakness***) and were described in subsection 5.5.1; results were compared between the two treatments and the significance level was $p \leq 0.05$. Treatments were independent but there was no replication; however, there the study was a regression design. Source of honeybees (*A. mellifera carnica*) was identified. The hives comprised three combs with queens from one line and had brood combs containing eggs, larvae and capped cells, ~8,000 to 10,000 bees per hive, 1-3 honey and pollen combs, and were free of disease. Dead bee traps (DBTs) were attached to the entrance of the hives. The hives were introduced to the tunnels on July 21, 2000 two months after sowing and at the start of full flowering and two days before assessment started to allow for acclimation. Measurement endpoints included honeybee mortality, flight intensity of bees in the tunnels, colony condition and development of bee brood, and honeybee behaviour. Methods for data collection were adequately described. The frequency of observations for mortality (Table 5) and flight intensity (Table 6) were reported for a duration of 10 days. Colony Quality and brood development was checked one day prior to placing the hives in the tunnels (July 20, 2000), once during exposure (July 31, 2000) and one week after the last evaluation (August 9, 2000) (p. 19).	**3**

	Samples were collected for residue analyses and included dead honeybees and leaves and blossoms of sOSR. No residue analyses or data were included (**major weakness**).	
Use of GLP and QA/QC.	The study followed GLP and included a statement of compliance, statement of quality assurance with proof of audits, study plan, deviations from study plan and plan amendments and was conducted by a GLP certified testing facility. Plots were independent but there was no replication just repeated measures over time.	**4**
Exposure concentrations	The confirmed rates of measured concentrations: 429.0, 814.1, 1265.4, 1686.3, 2487.4 and 3303.6 g a.s. TMX/100kg seeds. No concentrations were measured in bee-relevant matrices.	**1**
Transparency of data.	Summary and raw data were provided.	**4**
Number of samples and replication.	Number of samples was endpoint specific (e.g., mortality n = 10; brood assessment n = 3). There were 8 treatments (2 controls and 6 TMX treatments. The plots were independent but there was no replication.	**4**
Overall evaluation of methods		**3.20**
Score for expert judgment on quality of the study- no independent replication of treatments (**major weakness**); no statistical analysis of mortality, colony Quality, and behavior data (**major weakness**).	**0.25**	**0.80**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. In all test substance groups, the mean number of dead bees per tunnel/day (DBTs + Linens) was low during the entire observation period compared to the control groups (Figure 4 and Table 8; Tables 13-16; Appendix A2). The mean number of dead bees per tunnel during the observation period did not exceed 10 dead bees /tent/day. However, there was an increase (30 dead bees/day) in mortality in one of the hives (T5) at the 6 x AR (2487.4 a.s.TMX/100 kg seeds) which occurred on the first assessment after introducing the hives to the tunnels but not at the 8xAR (3303.6 a.s. TMX/100 kg seeds) (8 dead bees/d) so there was no concentration-response. Cumulative mortality for each treatment was plotted over the 12 d assessment period and the slopes could have been statistically compared but were not (Figure 5) because there was “no remarkable difference” observed.	**0**
Concentration- or dose-response	There was no concentration-response effect observed for mean mortality of honeybees.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Because the mortality was lower at the highest concentration relative to the penultimate concentration and because the mortality observed for T5 was not consistently higher across assessments, the mortality was not attributed to TMX. Error bars overlapped and the data were highly variable.	**0**
Mechanism and or mode of action of effect explained	No mechanism was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		**0**

Response 2. Effects on honeybee foraging activity		Score
Statistical significance of responses	Mean flight intensity (Figure 6 and Table 9), reflected by the mean number of bees on 25 flowers/day, indicated that within-hive variability for measurements over time was high and that treatment-related effects were not apparent. Statistical comparisons using only C1 as a suitable control group (Tables 17-19, Appendix 2; raw and summary data provided in Tables 20-27) indicated that there were significant differences among treatments. Flight intensity in T6 (8xAR) was significantly lower than that for T1-T5 for most assessments, and was reduced relative to that for C1 on two occasions (6 and 8 DAE). Other significant reductions occurred at concentrations (T2, 2xAR; T4, 4xAR) on days 8 and/or 10. Despite these reductions in flight intensity the response was non-monotonic and there was no correlation between responses and concentrations. The conclusion was that a slight reduction in foraging intensity could be related to TMX at the highest exposure concentration (8xAR).	**4**
Concentration- or dose-response	There was no concentration-response effect observed for mean mortality of honeybees.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	The reduction at 8x the maximum application rate could reduce the foraging intensity of honeybees which in turn might adversely affect colony Quality and brood development; however, data for colony Quality and brood development were not supportive.	**2**
Mechanism and or mode of action of effect explained	No mechanism was provided or proposed.	**0**
Overall evaluation of relevance (computed)		**1.50**
Overall evaluation of relevance (SEJ). Because the reduction in flight activity occurred only at an unrealistic concentration, the score for relevance was reduced.		**0**

Response 3-7. Effects on colony Quality – area of combs with bees, brood, eggs, larvae, capped brood cells		Score
Statistical significance of responses	No statistical analyses of data were conducted and no P or r^2 values were presented. There were no differences in brood development (eggs, larvae, capped cells), attributed to the influence of the TMX; hives developed in a similar manner in both the TMX and the Control treatments (Table 28, Appendix A2).	**0**
Concentration- or dose-response	There were no observed effects and a concentration-response was not observed.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8. Effects on honeybee behaviour		Score
Statistical significance of responses	No data, no statistical analyses of data, and no P or r^2 values were presented. No abnormal behaviour of the bees was observed between the TMX and Control treatments at any time during the period of assessment.	**0**

Concentration- or dose-response	There were no observed effects and a concentration-response was not observed.	**0**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 2, 2016

(Syngenta 2003b)
Report: Syngenta. 2003. Field Test: Side Effects of Sunflower Grown from Seeds Dressed with A-9700 B on Honey Bee (*Apis mellifera* L.) in Argentina. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1697 - A9700B. 52 p

And

(Syngenta 2003a)
Paper or report: Syngenta. 2003. Determination of Analytes Thiamethoxam (CGA 293343) and Its Metabolite CGA 322704 in or on Pollen, Nectar and Honey from Sunflower Collected in Study 991567. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1704. 10 p

The first report is an assessment of sowing a TMX-treated sunflower crop on honeybees. A reference field was treated with imidacloprid (Gaucho 60 FS); these data are not included in the WoE. The exposure and residue data are provided in the second report cited above and are covered in the WoE_{EXP}[41].

Responses 1-11: Quality of methods		Score
Experimental design and hypotheses	The study comprised two fields 2.1 and 2.2 ha in size, respectively, for one sown with TMX-treated sunflower seed (*Helianthus annuus*; var. Paraiso 20 G2) and one control field with TMX-free sunflower seed of the same variety, source and batch. The fields were located in the vicinity of Rafaela City, Santa Fe Province, Argentina (Figure 1, Appendix 3) and were ≥4 km apart. No imidacloprid had been used in the fields in the previous few years; previous planting history was provided. Sunflower seeds were treated with TMX (Cruiser 350 FS; A-9700 B) at a nominal rate of 210 g a.s./100 kg seed (Section 7.2). Application rate on seeds was measured. Seeds were not treated any fungicides. Reference seeds were treated with imidacloprid (Gaucho 60 FS). Seeds were sown with a Migra seeder with 5 units on December 28, 2000 at a rate of 56,584 seeds/ha. Meteorological conditions were recorded (temperature, relative humidity, rainfall and weather conditions) at a site within 1 km of the study field during the study (Table 13–14 and 19–21 in Appendix 1). Eighteen hives were used in the study, six in each of the test, the reference and the control treatments. Honeybees (*Apis mellifera*) were from a local commercial source and inspected and certified for health. Each hive contained a brood body with 6-8 brood frames and one honey body with at least 8 frames. Number of bees per hive was not stated. The hives were placed into the fields at the edge in two groups of three per field when the sunflowers started to bloom on February 21, 2001 (BBCH: 61-62). Flowering ended March 2, 2001; all bee hives were transported back to the source apiary on March 6, 2001 in a rural area near Bella Italia, Santa Fe Province, Argentina. The first group of three	**2**

[41] Syngenta. 2003. Determination of Analytes Thiamethoxam (CGA 293343) and Its Metabolite CGA 322704 in or on Pollen, Nectar and Honey from Sunflower Collected in Study 991567. Basel, Switzerland: Syngenta Ltd. (Unpublished Report). Report CGA293343_1704. 10 p

	hives were fitted with dead bee traps (Appendix 4) and the second set of 3 hives had pollen traps that were used for the collection of pollen from foraging honeybees. Linen sheets at the hive entrance and in the field (three locations) were also used to assess honeybee mortality (Figures 5–7, Appendix 3). Flight intensity was assessed two days after set up using 5 x 1 m^2 plots established across the fields (Figures 5–7; Appendix 3). Brood development and colony Quality were assessed by the beekeeper. Hive weights were recorded using a beam scale and all colonies were weighed twice (February 22, 2001 and March 6, 2001). Honeybee behaviour was assessed in front of the hive and in the field during mortality and foraging checks. Measurement endpoints included mortality, foraging activity and behaviour (data collection started 2 days after the hives were set up and continued for 9 days); and, colony condition and brood development (3 x on days 3, 13 and 49 days after the hives were set up). The last brood assessment was conducted in preparation of the hives for the winter. The methods used followed procedures recommended by EPPO (1992)[29] and SETAC (1995)[32]. Comparisons between the TMX and the Control groups were made but no statistical procedures were applied to the data (***major weakness***) so effects were based on professional judgement and interpretation of the data. Samples were collected between February 23 and March 2, 2001 for residue analyses. Samples collected were nectar and honey from two different hives, pollen from pollen traps, pollen from flower heads, and nectar from foragers. Collection & processing methods, storage conditions, and analytical methods were described with recoveries and detection limits provided; however, TMX was detected in the pollen collected from the flowers in the control treatment but not in the treated plants which was attributed to a labelling mix up but constitutes a major limitation it this WoE.	
Use of GLP and QA/QC.	The study was not conducted under GLP but a full protocol and QC was provided.	**2**
Exposure concentrations	There was only one application rate used in this study and the rate was verified analytically. Residues were measured but reported elsewhere (Syngenta, 2003 #123). There were no residues reported above the chronic NOAED of 10.6 ng/bee/d in the WoE_{EXP}.	**4**
Transparency of data.	All raw data were provided.	**4**
Number of samples and replication.	There was only one site per treatment but there were 6 pseudo-replicated hives per site, only one or two of which were sampled.	**1**
Overall evaluation of methods		**2.60**
Score for expert judgment on quality of the study- statistical procedures were not applied to the effects data and is identified as a ***major weakness***	**0.5**	**1.30**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. There were no TMX-related adverse effects on honeybee mortality. The average mortality between days 2-9 was 16.8	**0**

	and 46.6 dead bees/colony/d for the TMX and control treatments, respectively (Table 7).	
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		
Overall evaluation of relevance (SEJ).		

Response 2. Effects on honeybee flight intensity		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. No treatment related effects on honeybee foraging were observed (Table 8; Tables 19-21, Appendix 2). During the observation period, flight intensity was 2.8 and 3.5 bees/m^2/plot and day for the TMX and control treatments, respectively.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3-6. Effects on colony Quality - # of bees, presence of health queen & food stores (pollen and nectar)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. The variation observed for the area covered by food stores (honey and pollen) are within the normal range and no TMX-related effects were indicated (Table 9 and Figure 8A and 8B). All queens in both treatments were alive and healthy. The population density was also similar between treatments (Table 9 and Figure 8C).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7-9. Effects on colony Quality – brood development (eggs, larvae & capped cells)		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. Brood development was normal and similar between treatments and the fluctuations showed a normal pattern (Table 9 and Figure 9).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on colony Quality – hive weights		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided (Tables 10-11). The average weight of the colonies was 35.7 and 35.2 kg for the TMX and control treatments, respectively, on day 1. On day 13, the average weight was 34.2 and 33.8, respectively. There was no treatment related effect on hive weights and the average weight decrease over the exposure period was 3.9 and 4.1% for the control and TMX-exposed colonies, respectively.	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 11. Effects on honeybee behaviour		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. There were no abnormal behaviours observed during foraging or flying (Tables 12).	**0**
Concentration- or dose-response	There was only one TMX application rate to one site; therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**

Overall evaluation of relevance (SEJ).	

Narrative
There were no signs of honeybee intoxication and no adverse effects observed on the Qualitys of the colonies, condition of the queen and the bee brood development which could be attributed to the exposure of the hives to the TMX-treated crop.

Expert Judgement		
QA	Yes	May 19, 2016
SEJ	Yes	May 30, 2016

(Syngenta 2009a)
Report: Syngenta. 2009. Thiamethoxam (CGA293343): A Field Study with A9807C Treated Winter Oilseed Rape Seed, Investigating Effects on Honeybees (*Apis mellifera* L.) over Four Years in Alsace (France). Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9807C_10957. 470 p

And

(Syngenta 2009b)
Syngenta. 2009. Thiamethoxam (CGA293343): A Field Study with A9807C Treated Winter Oilseed Rape Seed, Investigating Effects on Honeybees (*Apis mellifera* L.) over Four Years in Northern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9807C_10958 - A9807C. 469 p

These studies are similar in design and only the locations differ. For this reason, they were combined. The results are separated in the discussion of relevance. The purpose of these studies was to determine the effects of annual exposure to winter oilseed rape (*Brassica napus* var. *napus*), treated as seed with a flowable concentrate mixture of thiamethoxam, metalaxyl-M and fludioxonil (321.3 g/L FS formulation referred to as A9807C), on honeybees under field conditions over a period of four years.

Responses 1-13: Quality of methods		**Score**
Experimental design and hypotheses	TMX-treated (321.3 g/L FS with metalaxyl-M and fludioxonil) and untreated winter oilseed rape were sown in the Alsace region (study 1) and the Picardie region (study 2) of France in late summer/autumn of each year starting in 2004. The fields were ~2 ha and 2-3 ha (studies 1 and 2, respectively) for each treatment (Table 9 and Figures 23-26). Details of the treated and control seed, drilling, crop maintenance and field sites were provided (Tables 5 to 9 and Subsection 3.5.2; Tables 75 and 77 for studies 1 and 2 respectively). Nominal drilling rates for study 1 were 2004: 5 kg/ha; 2005, 2006: 3 kg/ha; and, 2007: 3 - 5 kg/ha (due to late drilling time) (p. 26) and for study 2 were 2004-2006: 3 kg/ha; and, 2007: 3 - 5 kg/ha (due to late drilling time) (p. 25). The details of sowing in each year of the studies are summarized in Tables 76 to 83 and 78 to 85 for studies 1 and 2, respectively. Control fields were sown with seed treated with thiram (2005) and fludioxinil and metalaxyl-M (2006-2008). The pesticide use history of all field sites selected for these studies and all relevant agricultural practice data were provided (Tables 84 to 109 and 86 to 115, for studies 1 and 2, respectively). Field separation was between 1.8 and 7.5 km for study 1 and by 2 to 3.2 km for study 2. Honeybee colonies were used over the test period from spring 2005 to spring 2009. Every spring, at the start of flowering of the winter oilseed rape plants (BBCH 60–62; 0-20 % of flowers open), six bee colonies were placed at the edge of each treated and six at the control field plots (exposure phase). Before and after flowering the colonies were maintained at a monitoring site (i.e., a forest near Hegeney, in the region of Alsace, France), for over-wintering. The experimental phase started in spring 2005 (08 Apr 2005) with the arrival of the bee colonies at their monitoring site (over-wintering location) and ended with the assessment after over-wintering in spring 2009 (18 Mar	**3**

	2009). For study 1, in 2004/2005, the exposure phase was conducted in Meistratzheim (treatment and control), in 2005/2006 in Krautergersheim (treatment) and Meistratzheim (control), in 2006/2007 in Gertwiller (treatment) and Zellwiller (control) and in 2007/2008 in Sand (treatment) and Herbsheim (control). For study 2, in 2004/2005, the exposure phase was conducted near Vingre (treatment and control), in 2005/2006 near Retheuil (treatment and control), in 2006/2007 near Chelles (treatment) and Mortefontaine (control) and in 2007/2008 near Vingre (treatment) and Christophe á Berry (control). The same field plots were not used in successive years to mitigate fungal disease. Measurement endpoints included honeybee mortality, foraging activity, and behaviour of the bees which were assessed every day during the first 9 days of the exposure period and in the following period every second or third day up to end of exposure. An assessment of brood development was done at least once before the start of exposure and afterwards every 7 ± 2 days until the end of exposure. During time of exposure plant and honeybee samples were taken for analysis of residues of TMX and its metabolite clothianidin. At the end of flowering (BBCH 67-69) in each year, the bee colonies were relocated to an area without extensive agricultural crops attractive to bees and with minimal pesticide usage (monitoring location). Colony health and Quality as well as brood development were assessed regularly over the whole year of assessment except between October and March (overwintering phase). At different time points during the studies samples of bees and nectar were taken in each colony of both treatment groups for the analysis of *Nosema sp., Malpigamoeba melificae, Acarapsis woodi, Varroa destructor, Paenibacillus l*arvae and different viruses (e. g. DWV (deformed wing virus), SBV (sacbrood virus), KBV (Kashmir bee virus), ABPV (acute bee paralysis virus) and CBPV (chronic bee paralysis virus). Samples of nectar[2], pollen[1], and plant[1] material were also collected for residue analyses (TMX LOQ[1] = 1.0 µg/kg and TMX LOQ[2] = 0.5 µg/kg; clothianidin LOQ = 1.0 µg/kg). The source of the honeybee colonies and maintenance was provided and both studies started in 2005 with healthy colonies (one egg-laying queen and approximately 10 000 – 20 000 bees per colony), housed in one to two brood bodies (= brood chamber, at least 6 brood combs and 4-14 combs with a mixture of 'wet', 'dry' and/or food combs). Additional bodies were added to the top of the hive as the colony developed. A queen excluder was placed above the brood chamber. The hives were of the Zandermass type. The colonies were as similar to one another as possible (based on e.g. number of worker bees, age-structure and extent of brood) at start of the studies. Meteorological data was monitored at each site and provided (Tables 53-65); data from a weather station nearby were also provided (Tables 66-69). Endpoint-specific assessment methods were described in detail and frequencies reported (see Subsection 3.6). Pollen source identification was included. Sample collection and preparation methods for residue analyses were detailed as well as the analytical methods including sample handling, shipping and storage (Tables 115-118 and 121 to 125, for studies 1 and 2, respectively).	

	The influence of the TMX treatment on honeybees was evaluated by comparing the data of the test item treatment group with the control data. Unfortunately, no statistical analyses of the data were described and no P values or r^2 values reported (**major weakness**).	
Use of GLP and QA/QC.	These GLP studies were compliant honeybee field studies conducted following the guideline of the European and Mediterranean Plant Protection Organisation No. 170 (3) (OEPP/EPPO, 2001)[4].	**4**
Exposure concentrations	Seed loading was confirmed analytically (Appendix 3). Residues were measured in nectar, bee pollen and other materials with appropriate methodologies and LODs and LOQs.	**3**
Transparency of data.	Raw and summary data were provided.	**4**
Number of samples and replication.	There was one control and one treatment each year for 4 years. There were 6 hives per treatment each year (pseudo replication).	**2**
Overall evaluation of methods		**3.20**
Score for expert judgment: No statistical analyses of the data were described and no P values or r^2 values reported (**major weakness**).	**0.5**	**1.60**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data. No test item-related increase in mortality compared to the control was observed during the exposure period in the test fields in 2005, 2006, 2007 and 2008 (Figure 1). For study 1, in 2006, the number of dead bees in the colonies at the control field was on a higher level throughout the whole exposure period compared to the TMX-treated field. For study 2 in 2005, the number of dead bees in the colonies at the TMX-treated field was on a higher level throughout almost the whole exposure period compared to the control; however, it was still within the range which is normally recorded in honeybee colonies held under field conditions. In 2008, there was a similar trend, due to higher mortality in single colonies of the TMX-treated field, where other colonies were within the range of control colonies (Figure 7). Data are presented in Figures 1, and 7 and Tables 15-22.	**0**
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on flight intensity of honeybees		**Score**
Statistical significance of responses	No statistical procedures were applied to the data. The number of forager bees was sometimes higher in the control field or in the test item field (Figure 2), but no test item related difference was observed with three exceptions: 1) in study 1 during the exposure period in 2007	**0**

	where the flight intensity in the test item field was on a higher level than that recorded in the control, 2) in study 1 from day 6 to 12 of exposure in 2008, where the flight intensity in the control field was slightly higher than that recorded in the TMX-treated field, and 3) in study 2 during the exposure period in 2008 where flight intensity in the test item field was slightly higher than in the control field. At the end of the observation period the flight intensity decreased in both test fields for both studies (2005, 2006, 2007 and 2008) because the crop was coming to the end of its flowering period. For study 1, the daily mean flight intensity during time of exposure was 4.0 forager bees/m² (2005), 2.6 forager bees/m² (2006), 3.8 forager bees/m² (2007) and 1.8 forager bees/m² (2008) in the test item treated group and 5.1 forager bees/m² (2005), 2.7 forager bees/m² (2006), 2.7 forager bees/m² (2007) and 2.3 forager bees/m² (2008) in the control group (Tables 23-30). For study 2 the daily mean flight intensity during time of exposure was 1.9 forager bees/m² (2005), 1.2 forager bees/m² (2006), and 0.7 forager bees/m² (2007/2008) in the test item treated group and 1.8 forager bees/m² (2005), 1.0 forager bees/m² (2006), 0.7 forager bees/m² (2007) and 0.4 forager bees/m² (2008) in the control group.	
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Differences in flight intensity in the test fields recorded on single occasions were attributed to different conditions at the field sites rather than the treatments in the test fields.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3. Effects on honeybee behavior		**Score**
Statistical significance of responses	No statistical procedures were applied to the data. No behavioural differences of the bees in the TMX treatment group were observed during the entire exposure period to the crop compared to the honeybees in the control group in the four years of observations (Subsection 4.4, p 45 and p 43, for studies 1 and 2, respectively).	**0**
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-5. Effects on colony Quality – number of bees, brood nest size,	**Score**

Statistical significance of responses	No statistical procedures were applied to the data. The Quality of the colonies (number of bees in the hives – Figures 3 and 8; Tables 31-42 and 31 to 40, for studies 1 and 2, respectively) and the breeding activity (brood nest size; Table 31-42) showed approximately the same tendency to increase or decrease over the observation period from spring to autumn in 2005, 2006, 2007 and 2008. The colony Quality varied within the normal range expected. In study 2, the same general trend was observed except for spring 2006 and June 2007 to March 2009 the mean Quality of the colonies in the TMX treated field was higher than that in the control. This was due to a reduced number of bees in single colonies of the control (Figure 8 and Tables 31 to 40).	**0**
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on colony Quality – overwintering success		**Score**
Statistical significance of responses	No statistical procedures were applied to the data. No TMX related difference in Quality, breeding activity and survival of the colonies in the TMX treatment compared to the control colonies was observed during the experimental phase of the studies from spring 2005 up to end of over-wintering in 2009. Hive losses occurred across treatments equally.	
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7. Effects on colony health – pests, parasites, disease		**Score**
Statistical significance of responses	No statistical procedures were applied to the data. Assessments for disease occurred each year before, during and after exposure and during the monitoring phase with variable results summarized for each hive in Subsection 4.3.5. Although infestations ranged from minor to severe there was no temporal or spatial pattern to the differences. Overall no TMX-related differences regarding the colony health was observed during the entire test period	**0**

Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8. Effects on colony Quality – hive weight		**Score**
Statistical significance of responses	No statistical procedures were applied to the data (Figures 6 and 21). Due to different beekeeping activities (e.g. bee colony separation, adding of bodies, removing of combs, feeding of the colonies) and the natural development in the colonies, large increases and decreases in the mean weight of the colonies were observed over the four years of observations. Although the weights in study-1 for the TMX-treatment hives were consistently lower than those in the control treatment in 2007 (Figure 6) by the end of the season they were similar to those in the control treatment. Additionally, in 2008 one of the hives in the TMX treatment group was consistently lower than the others in the group and the control treatment. In study-2, from May 2007 to September 2008, the mean weight was slightly higher in the TMX treatment than in the control (approx. 8-10 kg). This was caused by a decreased weight in one colony of the control. These observed differences in 2007 and 2008 for both studies were not thought to be related to TMX. On the last assessment in 2009 for both studies, the mean weight of colonies in the TMX treated group and the control group were on similar levels.	**0**
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 9-13. Effects on colony health – brood development (comb area with eggs, larvae, pupae & food stores)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data (Tables 31-42 and 31 to 40, for studies 1 and 2, respectively) summarized in Figures 4-5 for the TMX and control treatment mean data, respectively, and in Figures 9-20 and 9 to 15 (for studies 1 and 2, respectively) for each hive across years and subsections 4.3.2 and 4.3.3. The % comb coverage of brood (eggs, larvae and pupae) and food (nectar and pollen) in the colonies showed approximately the same development	**0**

	between the TMX treatment and control groups in 2005, 2006, 2007 and 2008 (Figures 4 and 5). For study 2, from 2006 to 2007 three colonies of the test item group were observed with male brood in the autumn of 2006. After over-wintering in the spring of 2007, one colony died and the other two still showed male brood. The colonies were replaced in the spring of 2007, and thereafter no difference in the colony development was observed.	
Concentration- or dose-response	There was only one control and one TMX field for each year of the studies and because the application rates were similar among years, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

Over the observation period from spring 2005 to the 18th March 2009, it can be concluded that annual exposure of honeybees (*Apis mellifera* L.) to winter oilseed rape grown from seeds treated with a flowable concentrate mixture of TMX, metalaxyl-M and fludioxonil (321.3 g/L FS formulation referred to as A9807C) had no effect on the honeybee colony development (e.g. Quality, brood and food development, colony health, over-wintering success). Furthermore, no test item related differences on honeybee mortality, the flight intensity in the test fields and behaviour of the bees during the time of exposure to the winter oilseed rape fields were observed in 2005, 2006, 2007 and 2008. For study 1 a maximum residue level of 0.001 mg/kg (treated bee pollen) to 0.003 mg/kg (treated bee nectar) of TMX was detected in samples taken in the test item field from 2006 to 2008. A single residue of clothianidin was detected in the treated oilseed rape at a level of 0.001 mg/kg in 2007 and 2008. In the other treatment samples residues levels of clothianidin were below LOQ (0.001 mg/kg) or no measurable residues of clothianidin were detected. For study 2 TMX residue levels of 0.0007 mg/kg in bee nectar was detected in samples taken in the test item field from 2006 to 2008. No measurable residues of TMX were found in any other specimen and residues of clothianidin were all below LOQ (0.001 mg/kg) or no measurable residues of clothianidin were detected. No measurable residues of TMX or clothianidin were detected in any of the control specimens analyzed in study 1 or 2.

Expert Judgement		
QA	Yes	June 3, 2016
SEJ	Yes	June 5, 2016

(Syngenta 2010c)
Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Field Study with A9700B + A9638A Treated Maize Seed, Investigating Effects on Honeybees (*Apis mellifera* L.) over Four Years in Alsace (France). Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10911 - A9700B. 558 p

The purpose of the study was to determine the effects of annual exposure of honeybees to maize, treated as seed with a flowable concentrate mixture of TMX (thiamethoxam), metalaxyl-M and fludioxonil (from 2006 to 2008: 0.9 L A9700B + 0.1 L A9638A/100 kg seed; in 2009: 0.09 L A9700B/50 000 grains and 0.1 L A9638A/100 kg seeds), under field conditions over a period of four years (from 2006 to 2009).

Responses 1-14: Quality of methods		**Score**
Experimental design and hypotheses	TMX-treated (near La Petite Pierre) and TMX-free maize seed (var. Moncada – 2006; PR39G12 – 2007; NK Terrada – 2008; Aadhoc and NK Perform – 2009; p. 30) (near Puberg) were sown at a nominal seeding rate of 28 kg/ha in field plots (2 and 3 ha, respectively), in the region of Alsace, France. The two field plots were sown in the spring in each year from 2006 to 2009 on the same field plots. The two field plots were separated by approximately 5 km (to minimise the likelihood of bees from one treatment visiting the field plot of the other treatment). Selected field plots were isolated from other honeybee attractive crops flowering at the same time as the maize in the field plots within distance of 2 km to avoid a dilution in exposure to any potential residues of TMX. In 2009, the fourth year of the study, two different drilling dates with two different maize varieties (variety 1: LG AADHOC; variety 2: NK PERFORM) were chosen to extend the flowering period in the maize field plots and likewise the exposure period (to 24 d). Therefore, each field plot (control and treatment) was divided into four approximately equal parts, of which two pairs of the different varieties were drilled on the same day. Seed sources were identified (p. 30); seed loading rates confirmed (Tables 5-9) and certificates of analysis included (Appendices 5 & 6); drilling rates were also confirmed (Section 3.4.2 and Tables 10-25). Maintenance followed good agricultural practices and was well documented along with historical site conditions and land uses (p. 33; Tables 116-125). Meteorological data were recorded and reported (Tables 92-100) as well as physico-chemical characteristics of the soils (Table 115). Materials (plant, pollen from plants and foraging bees) were taken and analysed for residues of TMX and clothianidin. Maximum levels of 0.002 mg/kg (treated bee pollen) and 0.024 mg/kg (treated plant) of TMX and of 0.002 mg/kg (treated bee pollen) and 0.010 mg/kg (treated plant) for clothianidin were detected in samples taken in the TMX-treated field from 2006 to 2009. In 2007 and 2009, sufficient bee-collected pollen was not available so pollen from plants was analyzed for TMX and clothianidin residues. Residues of < 0.001 mg/kg for both, TMX and clothianidin were detected in all years. Hives (n = 6 for 2005-2008; n = 6+1 for pollen collection for 2009) comprising healthy colonies (one egg-laying queen and approximately 4 438 to 22,875 bees per colony), housed in two brood bodies (= brood chamber, 5-8 brood combs + 15-20 combs with a mixture of 'wet', 'dry' and/or food combs) were placed at the edge of the fields at the onset of flowering (BBCH 51-63) and remained there for the exposure period until	**4**

	the end of flowering in 2006 to 2008 or until the last variety had finished flowering in 2009 (~BBCH 69). Additional bodies were added to the top of the hive as the colony develops. A queen excluder was placed above the brood chamber. The colonies were as similar to one another, as possible (based on e.g. age structure and extent of brood). The exposure period was 6, 9, 6, and 24 days for years 2006 to 2009. In 2006, the hives were moved to a monitoring location near Drusenheim in the region of Alsace, FR for pre-mortality monitoring and thereafter to Haguenau in the same region for the rest of the monitoring phase. This area had little agriculture, with natural forage plants favourable to survival and colony fitness such as blackberry, golden rod, blueberry, grass, hazel, alder, robinia and pine trees (details of the surrounding flora were documented in the study file). Methods followed standard procedures (Imdorf et al. 1987)[3]. Effects on honeybees of exposure to TMX-treated crops was assessed repeatedly over time from the pre-exposure phase to the post-exposure monitoring phase and then after the overwintering phase in the subsequent spring. Measurement endpoints included colony Quality (number of adult bees, workers and drones); hive weights, health (pest, parasites and disease), and development (brood -egg, larvae, pupae; food-nectar and pollen); queen development; mortality; flight intensity and foraging activity; behaviour of bees; and overwintering success. Standard bee practises were invoked and the assessments conducted according to OEPP/EPPO (2001)[4]. No statistical analyses were applied to the results of the study and no P or r^2 values were provided (**major weakness**).	
Use of GLP and QA/QC.	GLP study; signatures, QA and GLP audits; QA statement, study plan, raw data, study plan deviations and amendments, certificates etc. Loading rates for seeds were confirmed analytically.	**4**
Exposure concentrations	Residues of TMX were detected in the treated maize plant specimens from 2006 to 2009 at concentrations between 1.26 to 24 µg/kg. Residues of clothianidin were detected in the treated maize plant specimens from 2006 to 2009 between 1.92 to 10 µg/kg. Residues of < 1 to 2 µg/kg for TMX and clothianidin were detected in the treated bee pollen sample from 2006 to 2008. In 2007 and 2009, due to insufficient bee pollen, the pollen from plants was analysed. Residues of <0.001 mg/kg for both, TMX and clothianidin were detected in both years. No residues of TMX and clothianidin above the LOQ were detected in any of the control samples (Appendices 3 and 4 for details). The LOQ was 1.0 µg/kg. Analytical confirmation of seed loadings (Tables 5-9) indicated that in 2006, the nominal seed loading was 0.816 mg TMX/seed and the actual was 0.800 mg/seed; in 2007, the nominal was 0.977 and the actual was 0.955 mg TMX/seed; in 2008, the nominal was 0.684 and the actual 0.736 mg TMX/seed; in 2009, the nominal for AADHOC variety was 0.63 and the actual 0.65 mg TMX/seed whereas for NK Perform the corresponding values were 0.63 and 0.64 mg TMX/seed, respectively. Seeding rates were also confirmed (Tables 10-25).	**4**
Transparency of data.	Raw data and summary data included.	**4**
Number of samples and replication.	There were 2 independent field plots one treated with TMX and one control. There were 6 hives per treatment and multiple assessment points over time. This was a multiyear project so the four years comprise	**3**

	independent replicates. Unfortunately, no statistical analyses of the data were applied (**major weakness**).		
Overall evaluation of methods			**3.80**
Score for expert judgment on quality of the study– no statistical analyses of the data were applied (***major weakness***)		**0.5**	**1.90**

Response 1. Effects on honeybee mortality – number of dead bees (traps/sheets)		**Score**
Statistical significance of responses	No statistical procedures were applied to the mortality data and no P values reported. The daily mean number of dead bees in front of the hives (dead bee traps and linen sheet) during the time of exposure was 13.8 (2006), 33.9 (2007), 4.2 (2008) and 6.5 dead bees/hive (2009) in the test item treated group and 13.6 (2006), 38.0 (2007), 6.1 (2008) and 6.4 dead bees/hive (2009) in the control group (Tables 31-38; Figure 1). Mortality was similar between treatments.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on flight intensity and foraging activity of honeybees		**Score**
Statistical significance of responses	No statistical procedures were applied to the foraging activity or flight intensity data and no P values reported. Over the four years of assessments, no test item related differences regarding the flight intensity or foraging activity were observed in the TMX-treated fields compared to the controls. Differences in flight intensity in the TMX-treated fields recorded on single occasions were caused by different conditions at the field sites rather than the treatments in the test fields (Tables 39-52; Figure 2).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		Score
Statistical significance of responses	No statistical procedures were applied to the behaviour data and no P values reported. No behavioural differences of the bees in the TMX-treated fields or treatment group were observed during the entire exposure period to the crop compared to the bees in the control group from 2006 to 2009 (Tables 53-60; Subsection 4.4, p. 62.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on colony Quality – number of bees		Score
Statistical significance of responses	No statistical procedures were applied to the data for number of bees and no P values reported. Figure 3 summarizes the mean colony Quality in terms of the number of honeybees per hive over the four years (Tables 61-71) and demonstrates similar Quality between the control and the TMX-treatment groups. Figure 8 summarizes the data for each hive over the four years and the variability is high and individual hives appeared to differ in Quality between the control and TMX treatment groups. No TMX-related difference in colony Quality in the test item treatment compared to the control colonies was observed during the experimental phase of the study from July 2006 up to March 2010. Differences that occurred were attributed to other causal variables (e.g. overwintering losses).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on colony health – pests, parasites and disease		Score
Statistical significance of responses	No statistical procedures were applied to the health data and no P values reported. At different time points during the study, samples of bees and nectar were taken in each colony of both treatment groups for the analysis of *Nosema* sp., *Malpigamoeba melificae, Acarapsis woodi, Varroa destructor, Paenibacillus larvae* and different viruses (e.g. DWV (deformed wing virus), SBV (sacbrood virus), KBV (Kashmir bee virus), ABPV (acute bee paralysis virus) and CBPV (chronic bee paralysis virus)). After the monitoring period 2006 to 2010 the results of the disease and virus analysis show that the test item treated colonies	**0**

	are as healthy as the control colonies (p.62). Data were summarized in independent reports (Appendices 1 (bee disease) and 2 (viruses)) and discussed for each year in Subsection 4.3.4 (p. 58).	
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response7. Effects on honeybee health – hive weights		**Score**
Statistical significance of responses	No statistical procedures were applied to the hive weight data and no P values reported. Mean maximum hive weights are summarized over time in Figure 6 with apparent treatment differences in 2008 and 2009 in the exposure period with recovery occurring by the end of the season. Data for each hive are in Tables 74-81. Due to different beekeeping activities (e.g. bee colony separation, adding of bodies, removing of combs, feeding of the colonies) and the natural development in the colonies, large increases and decreases in the mean weight of the colonies were observed over the four years of observations. However, during the first year of assessments no test item related difference could be observed but starting from May 2008 the colonies in the test item group were slightly behind the control colonies. It was thought that a better supply of flowering plants in the surrounding area of the control colonies at the monitoring location explained some of this variability.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8-13. Effects on colony Quality – brood development (brood nest; eggs, larvae, pupae) & food stores (honey and pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to the brood development and food stores data and no P values reported. The mean Quality of the colonies (brood nest size and development – egg, larvae, pupae; Figures 4 and 5) showed approximately the same tendency to increase or decrease over the observation period from spring/summer to autumn in 2006, 2007, 2008 and 2009 (Tables 61-73). No TMX-related differences compared to the control colonies were observed during the experimental phase of the study from spring 2006 up to end	**0**

	of over-wintering in 2010. The honeybee colony development in individual hives showed much variability (Figures 9-20) but generally Quality, brood and food development were similar between the treatment groups, especially in 2006, 2008 and 2009. In spring all colonies increased their breeding activity and had a good food supply from flowering plants. The amount of food stores on the combs increased likewise. Starting from the bee colony separation at end of the exposure period at the test fields (removing brood, store combs and the old queen in 2007 and 2008) a sharp decrease in the number of bees in hives combined with a lack of brood in both test groups was recorded.	
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 14. Effects on colony Quality – overwintering success		**Score**
Statistical significance of responses	No statistical procedures were applied to the overwintering success data and no P values reported. Three colonies died in the TMX-treatment group (2007/2008: T4, 2008: T3, 2008/2009: T5) and only one in the control group (2008: C3 died in the spring and the substitute of C3 again in the fall) over the four years of observations. There was no TMX-related adverse effects.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

Over the observation period from summer 2006 to the 25 March 2010, it can be concluded that four seasons of exposure of honeybees (*Apis mellifera* L.) to flowering maize grown from seeds treated with a flowable concentrate mixture of thiamethoxam, metalaxyl-M and fludioxonil had no adverse effects on honeybee mortality, the flight intensity and behaviour of the bees in the field was unaffected during the exposure period in all four years- 2006, 2007, 2008 and 2009. The honeybee colony development (e.g. Quality, brood and food development, overwintering success, colony health) was similar between the treatment groups, especially in 2006, 2008 and 2009. The weight of the control colonies was similar in 2006 and 2007 but starting from May 2008 the colonies in the test item group were slightly behind the control colonies which was

attributed to conditions at the monitoring locations for the control colonies had better access to flowering plants in the surrounding area or single colonies in the control treatment group were more effective in collecting food. **It was not considered to be a TMX-related adverse effect!**

Residues of TMX were detected in the treated maize plant specimens from 2006 to 2009 at concentrations between 1.26 to 24 µg/kg. Residues of clothianidin were detected in the treated maize plant specimens from 2006 to 2009 between 1.92 to 10 µg/kg. Residues of < 1 to 2 µg/kg for TMX and clothianidin were detected in the treated bee pollen sample from 2006 to 2008. In 2007 and 2009, due to unavailability of enough bee pollen, the pollen from plants was analysed. Residues of < 0.001 mg/kg for both, TMX and clothianidin were detected in both years. No residues of TMX and clothianidin above the LOQ (were detected in any of the control samples.

Expert Judgement		
QA	Yes	June 2, 2016
SEJ	Yes	June 5, 2016

(Syngenta 2010d)

Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Field Study with A9700B + A9638A Treated Maize Seed, Investigating Effects on Honeybees (*Apis mellifera* L.) over Four Years in Lorraine (France). Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10912 - A9700B. 527 p

The purpose of the study was to determine the effects of annual exposure of honeybees to maize, treated as seed with a flowable concentrate mixture of thiamethoxam, metalaxyl-M and fludioxonil (from 2006 to 2008: 0.9 L A9700B + 0.1 L A9638A/100 kg seed; in 2009: 0.09 L A9700B/50 000 grains and 0.1 L A9638A/100 kg seeds) under field conditions over a period of four years (from 2006 to 2009).

Responses 1-14: Quality of methods		Score
Experimental design and hypotheses	TMX-treated and TMX-free maize seed (var. Moncada – 2006; PR39G12 – 2007; NK Terrada – 2008; Aadhoc and NK Perform – 2009; p. 31) (Waville near Metz) were sown at a nominal seeding rate of 28 kg/ha in field plots (2 ha), in the region of Lorraine, France. The two field plots were sown in the spring in each year from 2006 to 2009 on the same field plots and the fields. The two field plots were separated by approximately 5 km (to minimise the likelihood of bees from one treatment visiting the field plot of the other treatment). Selected field plots were isolated from other honeybee attractive crops flowering at the same time as the maize in the field plots within distance of 2 km to avoid a dilution in exposure to any potential residues of TMX. In 2009, the fourth year of the study, two different drilling dates with two different maize varieties (variety 1: LG AADHOC; variety 2: NK PERFORM) were chosen to extend the flowering period in the maize field plots and likewise the exposure period (to 21 d). Therefore, each field plot (control and treatment) was divided into four approximately equal parts, of which two pairs of the different varieties were drilled on the same day. Seed sources were identified (p. 30); seed loading rates confirmed (Tables 5-9) and certificates of analysis included (Appendices 5 & 6); drilling rates and dates were also confirmed (Section 3.4.2 and Tables 10-26). Maintenance followed good agricultural practices and was well documented along with historical site conditions and land uses (p. 34; Tables 115-125). Meteorological data were recorded and reported (Tables 85-100) as well as physico-chemical characteristics of the soils (Table 115). Materials (plant, pollen from plants and foraging bees) were taken and analysed for residues of TMX and clothianidin. Maximum levels of <0.001 mg/kg (treated bee pollen) and 0.006 mg/kg (treated plant) of TMX and of <0.001 mg/kg (treated bee pollen) and 0.006 mg/kg (treated plant) for clothianidin were detected in samples taken in the TMX-treated field from 2006 to 2009. In 2007, 2008, and 2009 sufficient bee-collected pollen was not available so pollen from plants was analysed for TMX and clothianidin residues. Maximum residues of 0.001 mg/kg and 0.002 mg/kg for TMX and clothianidin were detected in all years. Hives (n = 6 for 2006-2008; n = 6+1 for pollen collection for 2009) comprising healthy colonies (one egg-laying queen and approximately 8,500 to 15,063 bees per colony), housed in two brood bodies (= brood chamber, 6-8 brood combs + 18-20 combs with a mixture of 'wet', 'dry'	**4**

	and/or food combs) were placed at the edge of the fields at the onset of flowering (2006: BBCH 53–63, 2007: BBCH 51-55, 2008: BBCH 61-65; 2009: BBCH 59-65) and remained there for the exposure period until the end of flowering (2006: BBCH 59-71; 2007; BBCH 63-65; 2008; BBCH 67-69; 2009: BBCH 65-(>69)). Additional bodies were added to the top of the hive as the colony developed. A queen excluder was placed above the brood chamber. The colonies were as similar to one another, as possible (based on e.g. age structure and extent of brood). The exposure period was 7, 10, 9 and 21 d for years 2006 to 2009. In 2006, the hives were moved to a monitoring location near Drusenheim in the region of Alsace, FR where pre-mortality was assessed and thereafter to Haguenau in the same region for the rest of the monitoring and overwintering. The monitoring area had little agriculture, with natural forage plants favourable to survival and colony fitness such as blackberry, golden rod, blueberry, grass, hazel, alder, robinia and pine trees (details of the surrounding flora were documented in the study file). Methods followed standard procedures (Imdorf et al. 1987)[3]. Effects on honeybees of exposure to TMX-treated crops was assessed repeatedly over time from the pre-exposure phase to the post-exposure monitoring phase and then after the overwintering phase in the subsequent spring. Measurement endpoints included colony Quality (number of adult bees, workers and drones); hive weights, health (pest, parasites and disease), and development (brood -egg, larvae, pupae; food-nectar and pollen); queen development; flight intensity and foraging activity; behaviour of bees; and overwintering success. Standard bee practises were invoked and the assessments conducted according to OEPP/EPPO (2001)[4]. No statistical analyses were applied to the results of the study and no P or r^2 values were provided (**major weakness**).	
Use of GLP and QA/QC.	GLP study; signatures, QA and GLP audits; QA statement, study plan, raw data, study plan deviations and amendments, certificates etc. Loading rates for seeds were confirmed analytically.	**4**
Exposure concentrations	A maximum residue level of 0.002 mg/kg (plant pollen) to 0.006 mg/kg (treated plant) of both, TMX and clothianidin was detected in samples taken in the test item field from 2006 to 2009. No measurable residues of TMX or clothianidin were detected in pollen from bees which was available only for 2006. No measurable residues of TMX or clothianidin were detected in any of the control samples analysed in this study (Appendices 3 and 4 for details). The LOQ was 1.0 µg/kg. Analytical confirmation of seed loadings (Tables 5-9) indicated that in 2006, the nominal seed loading was 0.816 mg TMX/seed and the actual was 0.805 mg/seed; in 2007, the nominal was 0.977 and the actual was 0.955 mg TMX/seed; in 2008, the nominal was 0.684 and the actual 0.736 mg TMX/seed; in 2009, the nominal for AADHOC variety was 0.63 and the actual 0.65 mg TMX/seed whereas for NK Perform the corresponding values were 0.63 and 0.64 mg TMX/seed, respectively. Drilling rates were also confirmed (Tables 10-26) for both treatments.	**4**
Transparency of data.	Raw data and summary data included.	**4**
Number of samples and replication.	There were 2 independent field plots one treated with TMX and one control. There were 6 hives per treatment and multiple assessment points over time. This was a multiyear project so the four years comprise independent replicates.	**3**

Overall evaluation of methods			**3.80**
Score for expert judgment on quality of the study – no statistical analyses of the data were applied (***major weakness***)		**0.5**	**1.90**

Response 1. Effects on honeybee mortality – number of dead bees (traps/sheets)		**Score**
Statistical significance of responses	No statistical procedures were applied to the mortality data and no P values reported. The daily mean number of dead bees in front of the hives (dead bee traps and linen sheet) during the time of exposure was 8.6 (2006), 19.5 (2007), 5.8 (2008) and 6.2 (2009) dead bees/hive in the test item treated group and 4.3 (2006), 11.4 (2007), 4.4 (2008) and 5.9 (2009) dead bees/hive in the control group (Tables 32-39; Figure 1). Mortality was similar between treatments and highly variable	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on flight intensity and foraging activity of honeybees		**Score**
Statistical significance of responses	No statistical procedures were applied to the foraging activity or flight intensity data and no P values reported. Over the four years of assessments, no test item related differences regarding the flight intensity or foraging activity were observed in the TMX-treated fields compared to the controls. In 2007 flight intensity in the control field was generally higher than that observed in the TMX-treated fields primarily because there was a delayed start of flowering in the control field (Tables 40-53; Figure 2). Differences observed on single occasions were caused by different conditions at the field sites rather than the TMX treatment.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour	**Score**

Statistical significance of responses	No statistical procedures were applied to the behaviour data and no P values reported. No behavioural differences of the bees in the TMX-treated fields or treatment group were observed during the entire exposure period to the crop compared to the bees in the control group from 2006 to 2009 (Tables 54-61; Subsection 4.4, p. 65).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on colony Quality – number of bees		**Score**
Statistical significance of responses	No statistical procedures were applied to the data for number of bees and no P values reported. Figure 3 summarizes the mean colony Quality in terms of the number of honeybees per hive over the four years (Tables 62-74) and demonstrates similar Quality between the control and the TMX-treatment groups. The mean Quality of the colonies (number of bees per colony) showed approximately the same tendency to increase and decrease from mid of July 2006 up to the last assessment in spring 2010. Figure 8 summarizes the data for each hive over the four years and the variability is high and, although individual hives appeared to differ in Quality between the control and TMX treatment groups on occasion. No TMX-related difference in colony Quality in the test item treatment compared to the control colonies was observed during the experimental phase of the study from July 2006 up to March 2010. Differences that occurred (Figure 8) were attributed to other causal variables (e.g. overwintering losses).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on colony health – pests, parasites and disease		**Score**
Statistical significance of responses	No statistical procedures were applied to the disease data and no P values reported. At different time points during the study, samples of bees and nectar were taken in each colony of both treatment groups for the analysis of *Nosema* sp., *Malpigamoeba melificae, Acarapsis woodi, Varroa destructor, Paenibacillus larvae* and different viruses (e.g. DWV (deformed wing virus), SBV (sacbrood virus), KBV (Kashmir bee virus), ABPV (acute bee paralysis virus) and CBPV (chronic bee	**0**

	paralysis virus)). After the monitoring period 2006 to 2010 the results of the disease and virus analysis show that the test item treated colonies are as healthy as the control colonies (p. 65). Data were summarized in independent reports (Appendices 1 (bee disease) and 2 (viruses)) and discussed for each year in Subsection 4.3.4 (p. 62).	
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7. Effects on honeybee health – hive weights		**Score**
Statistical significance of responses	No statistical procedures were applied to the hive weight data and no P values reported. Mean maximum hive weights are summarized over time in Figure 6 with no consistent treatment effect evident from 2006 and 2009 in the exposure period. There was one exception in 2008 in the pre-exposure period when the hive weight in one control hive was sufficiently high to necessitate colony separation. Data for each hive in each year are located in Tables 75-84. Due to different beekeeping activities (e.g. bee colony separation, adding of bodies, removing of combs, feeding of the colonies) and the natural development in the colonies, increases and decreases in the mean weight of the colonies were observed over the four years of observations. However, overall there was no treatment related adverse effects discernable.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8-13. Effects on colony Quality – brood development (brood nest; eggs, larvae, pupae) & food stores (honey and pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to the brood development and food stores data and no P values reported. The mean Quality of the colonies (brood nest size and development – egg, larvae, pupae; Figures 4 and 5) showed approximately the same tendency to increase or decrease over the observation period from spring/summer to autumn in 2006, 2007, 2008 and 2009 (Tables 62-74). The amount of food stores in combs followed similar patterns. No TMX-related differences compared to the control colonies were observed during the experimental phase of the study from spring 2006 up to end of over-	**0**

	wintering in 2010. The honeybee colony development in individual hives showed much variability (Figures 9-20) but generally Quality, brood and food development were similar between the treatment groups, especially in 2006, 2008 and 2009. In spring all colonies increased their breeding activity and had a good food supply from flowering plants.	
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 14. Effects on colony Quality – overwintering success		**Score**
Statistical significance of responses	No statistical procedures were applied to the overwintering success data and no P values reported. Six colonies died in the TMX-treatment group (2007: T5, 2007: T1, T4, T5 and T6, 2008: T3 and T4) and three in the control group (2008: C3 and C6, 2009: C5) over the four years of observations. There were no TMX-related adverse effects.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

Over the observation period from summer 2006 to the 26 March 2010 it can be concluded that four seasons of exposure of honeybees (*Apis mellifera* L.) to flowering maize from seeds treated with a flowable concentrate mixture of thiamethoxam, metalaxyl-M and fludioxonil (from 2006 to 2008: 0.9 L A9700B + 0.1 L A9638A/100 kg seed; in 2009: 0.09 L A9700B/50 000 grains and 0.1 L A9638A/100 kg seeds) had no effect on honeybee mortality, the flight intensity in the used test fields and behaviour of the bees during time of exposure to the maize fields in 2006, 2007, 2008 and 2009. The honeybee colony development (e.g. Quality, brood and food development, overwintering success, colony health) was similar between the treatment groups, especially in 2006, 2008 and 2009. Only after the bee colony separation in spring 2007, three of the colonies in the test item group showed male brood in the hives, which is an indicator that no fertile queen was in the colonies. In the affected colonies, the produced nuclei including the old queen was added to the origin colony and thereafter no difference in the colony development was observed between the treatments. **It was not considered to be TMX-related adverse effect!**

A maximum residue level of 0.002 mg/kg (plant pollen) to 0.006 mg/kg (treated plant) of both, TMX and clothianidin was detected in samples taken in the test item field from 2006 to 2009. No measurable residues of TMX or clothianidin were detected in pollen from bees which was available only for 2006. No measurable residues of TMX or clothianidin were detected in any of the control specimens analysed in this study. In 2009, due to unavailability of enough bee pollen, the pollen from plants was analyzed. Residues of 0.001 mg/kg for TMX and 0.002 mg/kg for clothianidin were detected.

Expert Judgement		
QA	Yes	June 2, 2016
SEJ	Yes	June 5, 2016

(Syngenta 2010h)

Report: Syngenta. 2010. Syngenta. 2010. Thiamethoxam (CGA293343) - A Field Study with A9700B + A9638A Treated Maize Seed, Investigating Effects on Honeybees (*Apis mellifera* L.) over Four Years in Southern France. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10913 - A9700B. 548 p

The purpose of the study was to determine the effects of annual exposure of honeybees to maize, treated as seed with a flowable concentrate mixture of thiamethoxam, metalaxyl-M and fludioxonil (from 2006 to 2008: 0.9 L A97 00B + 0.1 L A9638A/100 kg seed; in 2009: 0.09 L A9700B/50 000 grains and 0.1 L A9638A/100 kg seeds), under field conditions over a period of four years (from 2006 to 2009).

Responses 1-14: Quality of methods		Score
Experimental design and hypotheses	TMX-treated (near Gissac, Mas des Cols) and TMX-free maize seed (var. Dakovo – 2006; Justina – 2007; NX 1445 – 2008; Aadhoc and NK Perform – 2009; p. 29) (near Fayet Blancard) were sown at a nominal seeding rate of 28 kg/ha in field plots (~2 ha, respectively), in the region of Aveyron near Roquefort, in southern France. The two field plots were sown in the spring in each year from 2006 to 2009 on the same field plots and the fields. The two field plots were separated by approximately 12 km (to minimise the likelihood of bees from one treatment visiting the field plot of the other treatment). Selected field plots were isolated from other honeybee attractive crops flowering at the same time as the maize in the field plots by distance or a barrier (treeline or woodland) to avoid a dilution in exposure to any potential residues of TMX. In 2009, the fourth year of the study, two different drilling dates with two different maize varieties (variety 1: LG AADHOC; variety 2: NK PERFORM) were chosen to extend the flowering period in the maize field plots and likewise the exposure period (to 24 d). Therefore, each field plot (control and treatment) was divided into four approximately equal parts, of which two pairs of the different varieties were drilled on the same day. Seed sources were identified (p. 29); seed loading rates confirmed (Tables 5-9) and certificates of analysis included (Appendices 5 & 6); drilling rates and dates were also confirmed (Section 3.4.2 and Tables 10-24). Maintenance followed good agricultural practices and was well documented along with historical site conditions and land uses (p. 32; Tables 11-24 and Tables 116-125). Meteorological data were recorded and reported (Tables 83-99) as well as physico-chemical characteristics of the soils (Table 115). Materials (plant, pollen from plants and foraging bees) were taken and analysed for residues of TMX and clothianidin. A maximum residue level of 1 µg/kg (treated bee pollen) to 10 µg/kg (treated plant) of TMX and 2 µg/kg (treated bee pollen) to 8 µg/kg (treated plant) of clothianidin was detected in samples taken in TMX-treated field from 2006 to 2008. No measurable residues of TMX or clothianidin were detected in any of the control specimens analysed in this study. In 2009, due to unavailability of enough bee pollen, the pollen from plants was analysed. Residues of < 1 µg/kg for both, TMX and clothianidin, were detected. Hives (n = 6 for 2006-2008; n = 6+1 for pollen collection for 2009) comprising healthy colonies (one egg-laying queen and approximately 7,688 to 15,125 bees per colony), housed in two brood bodies (= brood	**4**

	chamber, 4-7 brood combs + 9-10 combs with a mixture of 'wet', 'dry' and/or food combs) were placed at the edge of the fields at the onset of flowering (BBCH 51–65) and remained at the exposure location until the end of flowering or until the last variety finished flowering (BBCH 51-71). Additional bodies were added to the top of the hive as the colony developed. A queen excluder was placed above the brood chamber. The colonies were as similar to one another, as possible (based on e.g., age structure and extent of brood). At the end of flowering the hives were relocated to Grenade/Garonne, in the region of Midi-Pyrénées, FR via Louslitges where pre-mortality and post-exposure colony Quality was assessed, for the rest of the monitoring phase and overwintering. The monitoring area has little agriculture and the surrounding flora consisted of wild flowering plants such as blackberry, golden rod, blueberry, grass, hazel, alder, robinia and pine trees in Louslitges and of pear, sunflower, hemp, plane tree, elder berry, maize, barley, rapeseed, wheat, sorghum, thorn apple and fallow in Meauzac (details of the surrounding flora were documented in the study file). Effects on honeybees of exposure to TMX-treated crops was assessed using standard methods (Imdorf et al. 1987)[3] repeatedly over time from the pre-exposure phase to the post-exposure monitoring phase and then after the overwintering phase in the subsequent spring. Measurement endpoints included colony Quality (number of adult bees, workers and drones); hive weights, health (pest, parasites and disease), and development (brood -egg, larvae, pupae; food-nectar and pollen); queen development; flight intensity and foraging activity; behaviour of bees; and overwintering success. Standard bee practises were invoked and the assessments conducted according to OEPP/EPPO (2001)[4]. No statistical analyses were applied to the results of the study and no P or r^2 values were provided (***major weakness***).	
Use of GLP and QA/QC.	GLP study; signatures, QA and GLP audits; QA statement, study plan, raw data, study plan deviations and amendments, certificates etc. Loading rates for seeds were confirmed analytically.	**4**
Exposure concentrations	A maximum residue level of 1 µg/kg (treated bee pollen) to 10 µg/kg (treated plant) of TMX and 2 µg/kg (treated bee pollen) to 8 µg/kg (treated plant) of clothianidin was detected in samples taken in the test item field from 2006 to 2008. No measurable residues of TMX or clothianidin were detected in any of the control samples analysed in this study. In 2009, due to insufficient bee pollen, the pollen from plants was analyzed. Residues of <1 µg/kg for both TMX and clothianidin were detected. Analytical confirmation of seed loadings (Tables 5-9) indicated that in 2006, the nominal seed loading was 1.074 mg TMX/seed and the actual was 1.095 mg/seed; in 2007, the nominal was 0.649 and the actual was 0.624 mg TMX/seed; in 2008, the nominal was 0.844 and the actual 0.914 mg TMX/seed; in 2009, the nominal for AADHOC variety was 0.63 and the actual 0.65 mg TMX/seed whereas for NK Perform the corresponding values were 0.63 and 0.64 mg TMX/seed, respectively. Drilling rates were also confirmed (Tables 10-24) for both treatments.	**4**
Transparency of data.	Raw data and summary data included.	**4**
Number of samples and replication.	There were 2 independent field plots one treated with TMX and one control in a single application. There were 6 hives per treatment and multiple assessment points over time. This was a multiyear project so the four years comprise independent replicates.	**3**

Overall evaluation of methods		**3.80**
Score for expert judgment on quality of the study – no statistical analyses of the data were applied (***major weakness***)	**0.5**	**1.90**

Response 1. Effects on honeybee mortality – number of dead bees (traps/sheets)		**Score**
Statistical significance of responses	No statistical procedures were applied to the mortality data and no P values reported. The daily mean number of dead bees in front of the hives (dead bee traps and linen sheet) during the time of exposure was 86.4 (2006), 20.7 (2007), 25.2 (2008) and 37.6 dead bees/hive (2009) in the test item treated group and 172.8 (2006), 61.2 (2007), 21.6 (2008) and 43.3 dead bees/hive (2009) in the control group (Tables 30-37; Figures 1 and 7). Mortality was similar between treatments though variable within individual hives.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on flight intensity and foraging activity of honeybees		**Score**
Statistical significance of responses	No statistical procedures were applied to the foraging activity or flight intensity data and no P values reported. Over the four years of assessments no test item related differences regarding the flight intensity or foraging activity were observed in the TMX-treated fields compared to the controls. The number of forager bees in the TMX-treated field was generally higher than, or similar to, that in the control field over the four years of assessments (Tables 38-51; Figure 2). Differences observed on single occasions were caused by different conditions at the field sites rather than the TMX treatment.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour	**Score**

Statistical significance of responses	No statistical procedures were applied to the behaviour data and no P values reported. No behavioural differences of the bees in the TMX-treated fields or treatment group were observed during the entire exposure period to the crop compared to the bees in the control group from 2006 to 2009 (Tables 52-59; Subsection 4.4, p. 60).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5. Effects on colony Quality – number of bees		**Score**
Statistical significance of responses	No statistical procedures were applied to the data for number of bees and no P values reported. Figure 3 summarizes the mean colony Quality in terms of the number of honeybees per hive over the four years (Tables 60-67 and Tables 70-72) and demonstrates similar Quality between the control and the TMX-treatment groups. The mean Quality of the colonies (number of bees per colony) showed approximately the same tendency to increase and decrease from mid of July 2006 up to the last assessment in March 2010. Figure 8 summarizes the data for each hive over the four years and the variability is high and, although individual hives appeared to differ in Quality between the control and TMX treatment groups on occasion, no consistent TMX-related difference in colony Quality in the TMX treatment compared to the control colonies was observed during the experimental phase of the study from July 2006 up to March 2010. Differences that occurred (Figure 8) were attributed to other causal variables (e.g. overwintering losses).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6. Effects on colony health – pests, parasites and disease		**Score**
Statistical significance of responses	No statistical procedures were applied to the disease data and no P values reported. At different time points during the study, samples of bees and nectar were taken in each colony of both treatment groups for the analysis of *Nosema* sp., *Malpigamoeba melificae, Acarapsis woodi, Varroa destructor, Paenibacillus* l*arvae* and different viruses (e. g. DWV (deformed wing virus), SBV (sacbrood virus), KBV (Kashmir	**0**

	bee virus), ABPV (acute bee paralysis virus) and CBPV (chronic bee paralysis virus). After the monitoring period 2006 to 2010, the results of the disease and virus analyses show that the test item treated colonies are as healthy as the control colonies (p. 60). Data were summarized in independent reports (Appendices 1 (bee disease) and 2 (viruses)) and discussed for each year in Subsection 4.3.4 (p. 56).	
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7. Effects on honeybee health – hive weights		**Score**
Statistical significance of responses	No statistical procedures were applied to the hive weight data and no P values reported. Mean maximum hive weights are summarized over time in Figure 6 with no consistent treatment effect evident from 2006 and 2009 in the exposure period. Data for each hive in each year are in Tables 73-82 and Figure 21. Due to different beekeeping activities (e.g. bee colony separation, adding of bodies, removing of combs, feeding of the colonies) and the natural development in the colonies, increases and decreases in the mean weight of the colonies were observed over the four year of observations. However, overall there were no treatment related adverse effects discernable.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8-13. Effects on colony Quality – brood development (brood nest; eggs, larvae, pupae) & food stores (honey and pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to the brood development and food stores data and no P values reported. The mean Quality of the colonies (brood nest size and development – egg, larvae, pupae; food – nectar and pollen Figures 4 & 5) showed approximately the same tendency to increase or decrease over the observation period from spring/summer to autumn in 2006, 2007, 2008 and 2009 (Tables 60-67, 70-72). Colony checks replaced every second more invasive brood assessments in 2009 (Tables 68-69). The amount of food stores in combs followed similar patterns. No TMX-related differences compared to the control colonies were observed during the	**0**

	experimental phase of the study from spring 2006 up to end of over-wintering in 2010. The honeybee colony development in individual hives showed much variability (Figures 9-20) but generally Quality, brood and food development were similar between the treatment groups, especially in 2006, 2007 and 2008. During the time of assessments in 2009, an unusual lack of brood was observed in single colonies of both treatment groups. Both treatment groups experienced adverse symptoms of chalkbrood, wax moth and mites in some colonies which might explain the lack of brood stages or queen losses from June 2008 to October 2009.	
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 14. Effects on colony Quality – overwintering success		**Score**
Statistical significance of responses	No statistical procedures were applied to the overwintering success data and no P values reported. Eleven colonies died in the TMX-treatment group (2006: T5, 2007: T1, T3 and T4, 2008: T5 and T6, 2009: T3 and T5, 2009/2010: T2, T3 and T5) and ten in the control group (2007: C1, 2008: C1, 2009: C3, C4 and C5, 2009/2010: C1, C2, C3, C4 and C5) over the four years of observations. There were no TMX-related adverse effects.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); approximately the same nominal application rate was used every year.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

Over the observation period from July 2006 to March 2010, it can be concluded that four seasons of exposure of honeybees (*Apis mellifera* L.) to flowering maize from seeds treated with a flowable concentrate mixture of TMX, metalaxyl-M and fludioxonil (from 2006 to 2008: 0.9 L A9700B + 0.1 L A9638A/100 kg seed; in 2009: 0.09 L A9700B/50 000 grains and 0.1 L A9638A/100 kg seeds) had no effect on the honeybee colony development (e.g. Quality, brood and food development, over-wintering success, colony health). Furthermore, no test item related differences compared to the control on honeybee mortality, the flight intensity in the used test fields and behaviour of the bees during time of exposure to the maize fields were observed.

A maximum residue level of 1.0 µg/kg (treated bee pollen) to 10 µg/kg (treated plant) of TMX and and 2 µg/kg (treated bee pollen) to 8 µg/kg (treated plant) of clothianidin was detected in samples taken in the test item field from 2006 to 2008. No measurable residues of TMX or clothianidin were detected in any of the control samples. In 2009, due to unavailability of enough bee pollen, the pollen from plants was analyzed. Residues of < 1.0 µg/kg for both TMX and clothianidin were detected.

Expert Judgement		
QA	Yes	June 2, 2016
SEJ	Yes	June 5, 2016

(Syngenta 2010k)
Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Semi-Field Study with A9700B + A9638A Treated Maize Seed, Followed by Untreated Flowering Crop(s), Investigating Residues in Crop(s), Soil and Honeybee Products in Picardie (France), in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10914 - A9700B. 184 p

A semi-field (use of tunnels in situ) study was conducted to determine the magnitude of residues of TMX (CGA293343) and its metabolite clothianidin (CGA322704) in crop, soil and honeybee products, following application of a flowable concentrate mixture of TMX (thiamethoxam) as a seed treatment for maize and then winter barley to evaluate potential exposure to honeybees, *Apis mellifera* L. A field planted with TMX-free maize and then winter barley served as an experimental control. Exposures via bee-relevant matrices are assessed in a separate WoE.

Responses 1-7: Quality of methods		**Score**
Experimental design and hypotheses	Maize (var. Nebora) pre-treated with the seed treatment TMX + A9638A was sown in a field plot near Appilly in the region Picardie, France in spring 2008 (Table 4). The rate of TMX applied was 76.80 g/ha. The maize planting was followed by a seeding of winter barley (var. Esterel) treated with TMX sown in the same field plot in autumn 2008. The rate of TMX applied with the barley seed dressing was 71.78 g/ha. The treated field plots were matched with a similar-sized control field plot sown with untreated seeds. In spring 2009, untreated flowering crops (alfalfa, sOSR and *Phacelia tanacetifolia*) were planted in both the treated and control field plots. Three different flowering crops were used: summer oilseed rape (sOSR - var. Ability), *Phacelia tanacetifolia* (var Angelia) and alfalfa (var. Marshal). The control and the treated field plots were split into four parts in spring 2009 (Figure 2) and separated by a buffer zone. The parts were large enough to accommodate 3 tunnels (size of 5 m x 40 m) with at least 2 m distance between each tunnel. The first seeding of each crop always was in the control. sOSR was drilled on March 20 and April 2, 2009; alfalfa drilled on April 2, 2009, and *Phacelia* on May 20, 2009. Prior to the onset of flowering, three tunnels were set-up on each flowering crop in the TMX-treatment field plots and one tunnel on each flowering crop in the control field plots and into each tunnel one bee colony (one queen, two brood bodies,10-20 combs, certified healthy) was placed during the flowering phase (Figure 3). The condition of the colonies and the development of the bee brood were assessed before introduction to the tunnel and once colonies were moved out of the tunnel. Samples of forager bees, whole plants of all three flowering crop species (oil seed rape, alfalfa and *P. tanacetifolia*) and soil were collected and sent for analysis of TMX and clothianidin analyses. Endpoints included as follow with methods adapted to (Imdorf & Gerig, 1999[2], and Imdorf et al., 1987)[3] cited rather than described: • Colony Quality • Presence of a healthy queen (e.g. presence of eggs) • Pollen storage area and area with nectar or honey (estimation adapted to • Area containing cells with eggs, larvae and capped cells.	**2**

	The condition of the colonies was checked once before set-up of the hives in the tunnels and once at the end of the exposure in the tunnels. At each assessment, the comb area containing bees and cells with nectar, pollen, eggs, larvae and capped cells were estimated per comb side. From this the total number of bees and cells containing the brood stages, pollen and nectar on the comb were calculated. This was done for all combs per hive. Mean values were calculated for each hive and assessment date (Tables 29 to 34). Source of hives was identified, structure and criteria for Quality parity provided (Subsection 3.3.3). Soil samples were collected for analyses for TMX and clothianidin residues (Table 35), temperature and precipitation records were provided (Figure 9 and 10, respectively), and TMX and clothianidin residues were measured in pollen collected by bees foraging on sOSR (Table 44), *Phacelia* (Table 43), alfalfa (Table 42). Foraging bees were enumerated and sampled in triplicate (Table 25) as well as whole plants (Table 26). There were no statistical procedures applied to the data and no P or r^2 values provided (**major weakness**). Methods for sample collection and experimental design were well described or cited. Specifications for the test material and details on drilling and crop maintenance provided as well as drilling rates which were verified (Subsection 3.2.1, p 18; Tables 8 and 9 for maize; Tables 11 and 12 for winter barley).	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures and etc.	**4**
Exposure concentrations	Single concentration was applied to maize and to winter barley. Residues were measured in plant material, nectar and pollen (see below).	**3**
Transparency of data.	Raw and summary data were provided in the report and appendices.	**4**
Number of samples and replication.	There were two treatments (fields) – one control and one TMX treatment; each TMX field was divided into 4 parts and planted with either sOSR (2 parts), alfalfa (1 part) or *Phacelia* (1 part). Tunnels were placed onto each part and each tunnel had one honeybee hive so there were triplicate hives for TMX and only one for each control part. Sample sizes were relatively small (n = 3) and the exposure period 5 days.	**2**
Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- There were no statistical procedures applied to the data and no P or r^2 values provided (**major weakness**).	**0.5**	**1.50**

Response 1. Effects on colony Quality – number of adult bees		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. The Quality of the colonies (estimated number of adult bees inside the hive) for all crops was between 6,138 and 20,319 bees per hive before the colonies were moved into the tunnels. After the colonies were moved out Quality was between 9,385 and 17,197 adult bees per hive. One of the hives placed in the *Phacelia* died during transport from the field. The average numbers in alfalfa and *Phacelia* increased while the numbers in oilseed rape decreased (Tables 29-34). No adverse effect was discerned.	**0**

Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Responses 2-7. Effects on colony Quality – brood development (# of combs with brood, number of cells with eggs, larvae, pupae (capped brood), food -nectar, pollen)		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r2 values provided. The number of eggs in the hives declined from the brood assessment before the study to the time when the hives were assessed at the end of the test. More eggs were found in one hive of one treatment tunnel in alfalfa. The number of larvae did not decrease as strongly as the eggs. There were two treatment tunnels in alfalfa and sOSR crop where the number of larvae increased between the two brood assessments. For the *Phacelia* numbers of larvae increased only in the control tunnel. For the cells with capped brood there was a general reduction, but numbers increased in all three flowering crops for one treatment tunnel. The lack of statistical analyses of these data and the fact that the few (n = 3) assessments were completed over a relatively short period of time precludes drawing definitive conclusions regarding effects of TMX.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

TMX effects or lack thereof were inconclusive; the focus of the study was on residues in soil, plant material, nectar and pollen. There were no TMX residues measured in pollen or nectar collected by bees in spring oilseed rape (sOSR) as a follow-on crop to maize and barley grown from TMX-dressed seeds that were above the chronic NOAED for honey bees of 8.6 ng/bee/d (WoE_{EXP}). TMX concentrations in pollen and nectar of sOSR determined from the 90th centile (n = 36 and 33, respectively) were 8.6 and 3 µg/kg or µg/L, respectively. Similarily, there were no TMX residues measured in the pollen or nectar collected by bees in *Phacelia* as a follow-on crop to maize and barley grown from TMX-dressed seeds that were above the chronic NOAED for honey bees of 8.6 ng/bee/d (WoE_{EXP}). TMX concentrations in pollen and nectar of *Phacelia* determined from the 90th centile (n = 20 and 36, respectively) were 4.5 and 0.95 µg/kg or µg/L, respectively. TMX and clothianidin residues in pollen and nectar collected by bees from alfalfa

as a follow-up crop to maize and barley grown from TMX-dressed seed were below the LOQ (<0.001 mg/kg).

Expert Judgement		
QA	Yes	May 30, 2016
SEJ	Yes	June 1, 2016

(Syngenta 2010j)
Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Semi-Field Study with A9700B + A9638A Treated Maize Seed, followed by Untreated Flowering Crop(s), Investigating Residues in Crop(s), Soil and Honeybee Products in Alsace (France), in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10915 - A9700B. 184 p

A semi-field (use of tunnels *in situ*) study was conducted to determine the magnitude of residues of TMX (CGA293343) and its metabolite clothianidin (CGA322704) in crop, soil and honeybee products, following application of a flowable concentrate mixture of TMX (thiamethoxam) as a seed treatment for maize and winter barley to evaluate potential exposure to honeybees, *Apis mellifera* L. A field planted with TMX-free maize and barley served as an experimental control. Exposures via bee-relevant matrices are assessed in a separate WoE_{EXP}.

Responses 1-7: Quality of methods		**Score**
Experimental design and hypotheses	Maize (var. Nebora) pre-treated with the seed treatment TMX (thiamethoxam-A9700B + A9638A) was sown (target seed rate- 28 kg/ha) in a field plot near Drusenheim in the Alsace region of France (Tables 2 and 4) in spring 2008 (April 28, 2008). TMX application was nominal 220.5 g TMX per 100 kg seed (actual 287 g/100 kg seed). The maize was followed by a seeding of winter barley (var. Esterel) treated with TMX only sown (target seeding rate- 110 kg/ha; Table 5)) in the same field plot in autumn (September 29, 2008). The nominal rate of TMX applied with the seed dressing was at approximately 70 g TMX/100 kg seed (actual 66.4 g/100 kg seed; Table 3). The treated field plots were matched with a similar size control field plot sown on with untreated seed (Tables 8, 11, 14, 17, 20 and 23). In spring 2009, the fields (TMX and control fields) were divided into four parts (Figure 2) and planted with untreated flowering crops (alfalfa – var. Marshal; summer oilseed rape (sOSR) - var. Ability) and *Phacelia tanacetifolia* – var. Angelia) on April 3, 2009, March 23 and April 3, 2009, and May 4, 2009, respectively. Two parts were planted with sOSR, 1 with alfalfa and 1 with *Phacelia*. Seedling rates and methods including calibration of drilling machines were provided and followed good agricultural practices. No products containing neonicotinoids were applied during the study period; historical pesticide use was known and no neonicotinoid insecticides or seed treatments were used in the field plots in at least the previous cropping season before use. This was confirmed by residue analysis of the soil taken before application. Loading and drilling rates were verified (Tables 8 and 9 for maize; Tables 11 and 12 for winter barley). Meteorological data were provided (Tables 27 and 28; Figures 9 and 10). Soils were characterized and chemically analysed for TMX residues. Prior to the onset of flowering, three tunnels were set-up on each flowering crop in the treated field plot and one tunnel on each flowering crop in the control field plot (Figure 3). In each tunnel one bee colony (one queen, two brood bodies,10-20 combs, certified healthy) was placed during the flowering phase (~7 days). The condition of the colonies and the development of the bee brood were assessed before introduction to the tunnel and once colonies were moved out of the tunnels (n = 2) following cited methodologies. Endpoints included the following with methods cited rather than described:	**2**

	• Colony Quality (number of bees, estimation adapted to Imdorf & Gerig, 1999[2], and Imdorf et al., 1987)[3] • Presence of a healthy queen (e.g. presence of eggs) • Pollen storage area and area with nectar or honey (estimation adapted to Imdorf & Gerig, 1999[2], and Imdorf et al., 1987[3] • Area containing cells with eggs, larvae and capped cells (estimation adapted to Imdorf & Gerig, 1999[2], and Imdorf et al., 1987)[3]. At each assessment (n = 2) the comb area containing bees and cells with nectar, pollen, eggs, larvae and capped cells were estimated per comb side. From this, the total number of bees and cells containing the brood stages, pollen and nectar on the comb were calculated. This was done for all combs per hive. Mean values were calculated for each hive and assessment date (Tables 29 to 34). Source of hives was identified, structure and criteria for Quality parity provided (Subsection 3.3.3). There were no statistical procedures applied to the data and no P or r^2 values provided (***major weakness***). Methods for sample collection and experimental design were well described or cited. Specifications for the test material and details on drilling and crop maintenance provided as well as drilling rates which were verified (Subsection 3.2.1, p. 17; Tables 8 and 9 for maize; Tables 11 and 12 for winter barley).	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures and etc.	**4**
Exposure concentrations	Single concentration was applied to maize and to winter barley. Residues were measured in plant material, nectar and pollen (see below) of subsequent crops grown on site.	**3**
Transparency of data.	Raw and summary data were provided in the report and appendices.	**4**
Number of samples and replication.	There were treatments (fields) – one control and one TMX treatments; each TMX and control field was divided into 4 parts and planted with either sOSR (2 parts), alfalfa (1 part) or *Phacelia* (1 part). Tunnels were placed onto each part and each tunnel had one honeybee hive so there were triplicate hives for TMX and only one for each control part. Sample sizes were relatively small (n = 1-3) and the exposure period 5 d.	**2**
Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- There were no statistical procedures applied to the data and no P or r^2 values provided (**major weakness**).	**0.5**	**1.50**

Response 1. Effects on colony Quality – number of adult bees		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. The Quality of the colonies (estimated number of adult bees inside the hive) for all crops was between 7,196 and 21,506 bees per hive before the colonies were moved into the tunnels. After the colonies were moved out Quality was between 4,572 and 20,259 adult bees per hive (Tables 29-34). No adverse effect was discerned.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**

(survival and/or reproduction, and fitness)		
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Responses 2-7. Effects on colony Quality – brood development (# of combs with brood, number of cells with eggs, larvae, pupae (capped brood), food -nectar, pollen)		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r2 values provided. The number of brood in the hives declined for oilseed rape and alfalfa but not as clearly for *Phacelia* despite the high number (Tables 29-34). This is a result that is expected in standard bee tunnel tests. There was no analysis of these data and the lack of statistical analyses and the fact that the only 2 assessments were completed over a relative short period of time precludes drawing definitive conclusions regarding effects of TMX.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

TMX effects or lack thereof were inconclusive; the focus of the study was on residues in soil, plant material, nectar and pollen. There were no TMX residues measured in pollen or nectar collected by bees in spring oilseed rape (sOSR) as a follow-on crop to maize and barley grown from TMX-dressed seeds that were above the chronic NOAED for honey bees of 10.6 ng/bee/d (WoE_{EXP}). TMX concentrations in pollen and nectar of sOSR determined from the 90th centile (n = 29 and 24, respectively) were 2.5 and 1.3 µg/kg or µg/L, respectively. Similarily, there were no TMX residues measured in the pollen or nectar collected by bees in *Phacelia* as a follow-on crop to maize and barley grown from TMX-dressed seeds that were above the chronic NOAED for honey bees of 10.6 ng/bee/d (WoE_{EXP}). TMX concentrations in pollen and nectar of *Phacelia* determined from the 90th centile (n = 32 and 36, respectively) were 7.6 and <LOQ µg/kg or µg/L, respectively. TMX and clothianidin residues in pollen (n = 1 pooled sample) and nectar (n = 36) collected by bees from alfalfa as a follow-up crop to maize and barley grown from TMX-dressed seed were 53.3 and <LOQ (<0.001 mg/kg). No residues of TMX or clothianidin above the LOQ were detected in any of the control summer oilseed rape nectar or pollen samples. No residues of TMX or clothianidin above the LOQ were detected in most control *Phacelia* pollen samples; however, there were detections above the LOQ; this was attributed to contamination during sample preparation (WoE_{EXP}).

Expert Judgement		
QA	Yes	May 30, 2016

SEJ	Yes	May 31, 2016

(Syngenta 2010b)
Report: Syngenta. 2010. Thiamethoxam (CGA293343) - A Semi-Field Study with A9700B + A9638A Treated Maize Seed, Followed by Untreated Flowering Crop(s), Investigating Residues in Crop(s), Soil and Honeybee Products in Burgundy (France), in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10916 - A9700B. 154 p

A semi-field (use of tunnels in situ) study was conducted to determine the magnitude of residues of TMX (CGA293343) and its metabolite clothianidin (CGA322704) in crop, soil and honeybee products, following application of a flowable concentrate mixture of TMX (thiamethoxam) as a seed treatment for maize and winter barley to evaluate potential exposure to honeybees, *Apis mellifera* L. A field planted with TMX-free maize and barley served as an experimental control. Exposures via bee-relevant matrices are assessed in a separate WoE.

Responses 1-7: Quality of methods		**Score**
Experimental design and hypotheses	Maize (var. Nebora) pre-treated with the seed treatment TMX (thiamethoxam-A9700B + A9638A) was sown (nominal and actual target seed rates- 28 and 20.9 kg/ha) with a Monosem drill in a field plot near Saint Cyr in the Burgundy region of France (Tables 2 and 4) in spring 2008 (May 15, 2008). TMX application was nominal 220.5g TMX per 100 kg seed (actual 287 g/100 kg seed). The maize was followed by a seeding of winter barley (var. Esterel) treated with TMX only sown (target seeding rate- 110 kg/ha; Table 5) in the same field plot in autumn (November 27, 2008). The nominal rate of TMX applied with the seed dressing was at approximately 70 g TMX/100 kg seed (actual 66.4 g/100 kg seed; Table 3). The treated field plots were matched with a similar size control field plot sown (maize – 24.05 kg/ha; barley – 116.5 kg/ha) with untreated seed (Tables 8 and 11). The seeding rates for subsequent plant crops were provided in Tables 14, 16, 18 and 20. In spring 2009, the fields (TMX and control fields) were divided into four parts (Figure 2) and planted with untreated flowering crops (alfalfa – var. Marshal; summer oilseed rape (sOSR) - var. Ability) and *Phacelia tanacetifolia* – var. Angelia) on April 6, 2009, March 25 and April 6, 2009, and May 12, 2009, respectively. Two parts were planted with sOSR, 1 with alfalfa and 1 with *Phacelia*. Seedling rates and methods including calibration of drilling machines were provided and followed good agricultural practices. No products containing neonicotinoids were applied during the study period; historical pesticide use was known and no neonicotinoid insecticides or seed treatments were used in the field plots in at least the previous cropping season before use. This was confirmed by residue analysis of the soil taken before application. Loading and drilling rates were verified (Tables 8 and 9 for maize; Tables 11 and 12 for winter barley). Meteorological data were provided (Tables 24 and 25; Figures 9 and 10). Soils were characterized and chemically analysed for TMX residues. Prior to the onset of flowering, four tunnels were set-up on each flowering crop in the treated field plot and one tunnel on each flowering crop in the control field plot (Figure 3-5). In each tunnel one bee colony (one queen, two brood bodies,10-20 combs, certified healthy) was placed during the flowering phase (~7 days). The condition of the colonies and the development of the bee brood were assessed before introduction to the tunnel and once colonies were moved out of the tunnels (n = 2) following cited methodologies (see footnotes). Triplicate	**2**

	samples of forager bees (nectar and pollen), whole plants of all flowering crop species (alfalfa, sOSR and *P. tanacetifolia*) and soil samples were collected for residue analysis of TMX and its metabolite clothianidin on three separate occasions. sOSR was excluded from the study in terms of effects because of damage inflicted by pollen beetle in the tunnels. Endpoints included as follow with methods cited rather than described: • Colony Quality (number of bees, estimation adapted to Imdorf & Gerig, 1999[2], and Imdorf et al., 1987)[3] • Presence of a healthy queen (e.g. presence of eggs) • Pollen storage area and area with nectar or honey (estimation adapted to Imdorf & Gerig, 1999[2], and Imdorf et al., 1987[3] • Area containing cells with eggs, larvae and capped cells (estimation adapted to Imdorf & Gerig, 1999[2], and Imdorf et al., 1987)[3]. At each assessment (n = 2) the comb area containing bees and cells with nectar, pollen, eggs, larvae and capped cells were estimated per comb side. From this, the total number of bees and cells containing the brood stages, pollen and nectar on the comb were calculated. This was done for all combs per hive. Mean values were calculated for each hive and assessment date (Tables 26 to 31). Source of hives was identified, structure and criteria for Quality parity provided (Subsection 3.3.3). Soil samples were collected for analyses for TMX and clothianidin residues (Table 32) from control and TMX treatments, temperature and precipitation records were provided (Tables 24 and 25; Figure 9 and 10, respectively). There were no statistical procedures applied to the data and no P or r^2 values provided (***major weakness***). Methods for sample collection and experimental design were well described or cited. Specifications for the test material and details on drilling and crop maintenance provided as well as drilling rates which were verified (Subsection 3.2.1, p. 18; Tables 8 and 9 for maize; Tables 11 and 12 for winter barley).	
Use of GLP and QA/QC.	GLP study with study plan, deviations, amendments, full QA/QC with audits and certifications, signatures and, etc.	**4**
Exposure concentrations	Single concentration was applied to maize and to winter barley. Residues were measured in plant material, nectar and pollen (see below) of subsequent crops grown on site.	**3**
Transparency of data.	Raw and summary data were provided in the report and appendices.	**4**
Number of samples and replication.	There were treatments (fields) – one control and one TMX treatments; each TMX and control field was divided into 4 parts and planted with either sOSR (2 parts), alfalfa (1 part) or *Phacelia* (1 part). Tunnels were placed onto each part and each tunnel had one honeybee hive so there were triplicate hives for TMX and only one for each control part. Sample sizes were relatively small (n = 1-3) and the exposure period 5 days.	**2**
Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- There were no statistical procedures applied to the data and no P or r^2 values provided (**major weakness**).	**0.5**	**1.50**

Response 1. Effects on colony Quality – number of adult bees		Score
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. The Quality of the colonies (estimated number of adult bees inside the hive) for all crops was between 11,449 and 23,318 bees per hive before the colonies were moved into the tunnels. After the colonies were moved out, Quality was between 10,444 and 25,635 adult bees per hive (Subsection 4.5, p. 27). The average number of bees per hive in *Phacelia tanacetifolia* increased while the numbers in alfalfa decreased (Tables 26-31). No adverse effect was discerned.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied each to two crops (maize and barley); two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Responses 2-7. Effects on colony Quality – brood development (# of combs with brood, number of cells with eggs, larvae, pupae (capped brood), food -nectar, pollen)		Score
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r2 values provided. The number of eggs, larvae and capped brood in the hives decreased for most of the hives. This is a result expected in standard bee tunnel tests. (Tables 26-31). There was no analysis of these data and the lack of statistical analyses and the fact that the only 2 assessments were completed over a relatively short period precludes drawing definitive conclusions regarding effects of TMX.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied to two crops in one treatment; two fields – control and TMX treatments.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

TMX effects or lack thereof were inconclusive; the focus of the study was on residues in soil, plant material, nectar and pollen. There were no TMX residues measured in the pollen or nectar collected by bees in *Phacelia* as a follow-on crop to maize and barley grown from TMX-dressed seeds that were above the chronic NOAED for honey bees of 8.6 ng/bee/d (WoE_{EXP}). TMX concentrations in pollen and nectar of *Phacelia* determined from the 90th centile (n = 34 and 36,

respectively) were 2.3 and <LOQ µg/kg or µg/L, respectively. No residues of TMX in nectar (n = 25) collected by bees from alfalfa as a follow-up crop to maize and barley grown from TMX-dressed seed were detected above the <LOQ (<0.001 mg/kg) (WoE_{EXP}). Spring oilseed rape samples were not measured.

Expert Judgement		
QA	Yes	May 30, 2016
SEJ	Yes	May 31, 2016

(Thompson et al. 2016)
Paper: Thompson H, Coulson M, Ruddle N, Wilkins S, Harkin S. 2016. Thiamethoxam: Assessing flight activity of honeybees foraging on treated oilseed rape using radio frequency identification technology. Environmental Toxicology and Chemistry 35:385-393.

This study was designed to assess homing behavior of bees foraging on winter oilseed rape grown from seed treated with thiamethoxam (as Cruiser OSR), with 1 field drilled with thiamethoxam-treated seed and 2 control fields drilled with fungicide-only treated seed. Honeybee activity was monitored using RFID transponders. Under the experimental conditions, there was no effect of foraging on thiamethoxam-treated oilseed rape on honeybee flight activity or on their ability to return to the hive.

Responses 1-4: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted on the east coast of the UK (Lincolnshire). Fungicides- and TMX-treated seeds were planted in October 2012 in one field and fungicide-only treated seeds in the 2 control fields. The crop was winter oilseed rape (var. Cabernet). The fungicides were fludioxinil and metalaxyl-M. The dressed concentration was 420 g TMX/100 kg seed or 0.020 mg TMX/seed. The drilling rate was 4.11 kg seed/ha and 4.15 kg seed/ha on the control and TMX-treated sites, respectively. Twelve honeybee colonies were used per treatment group, 4 each located at the field edge (on-field site), at approximately 500 m and 1000 m from the field. 36 queen-right honey bee (*Apis mellifera* L.) colonies, each with ~5,000 honey bees, were allocated randomly to three apiary sites per study field (on-field, at 0.5 km and 1 km from the field); each apiary site had four hives. The hive comprised 11 frames including 3 frames with brood. The RFID readers were established at the hive entrance. Historical use indicated that no neonicotinoids had been used on the fields in the last two years. General health of colonies selected for use in the study was good. The hives were moved to the sites when the crop on the least developed (treated) field had reached ~20% flowering. Endpoints measured included monitoring bee activity once per day by walking a ~100 m x 1 m transect with flowers within a randomly chosen section of the crop over a 10-min period. The numbers, species and behaviour of bees were recorded. A total of 273 bees per colony were fitted with transponders over three cohorts (100, 100, and 73). Movement into and out of the hives was recorded over a 5 wk period (16 May–20 June 2013). Onsite temperature and humidity were measured using dataloggers (Tinytag®) and other meteorological data from local stations were collected and recorded. During the peak of flowering, pollen was collected from bees returning to the hive on two occasions as well as from the hives themselves for palynological analyses using described methods. Bee disease was measured because of the influence of disease on foraging activity by collecting 100 adult honeybees on each of two occasions from each hive. DNA and RNA were extracted and analysed. Methods were well described with QA to determine extraction efficiency. Eleven pathogens were screened for using real-time reverse-transcriptase PCR. Pollen and nectar samples were collected from the crop plants in each field by hand and residues of TMX and the metabolite clothianidin measured using cited	**2**

	methods (Pilling et al. 2013)[42]; LOQ were 0.5 µg/kg nectar and 1 µg/kg pollen. Oilseed rape pollen was the most prevalent pollen identified in the corbicular samples with a couple of exceptions (p 388). The experimental design, despite the sample sizes, was such that the independent experimental units were the treatments (n = 3) (weakness). No statistical procedures were applied to the data and no P or r^2 values were provided (**major weakness**). Complete datasets for the RFID data were available only for 2 or 3 colonies at each site because of reliability problems associated with the dataloggers. Only complete datasets were used and data for "drifting bees" was not included in the analysis.	
Use of GLP and QA/QC.	Non-GLP study but methods well described with some QA included.	**2**
Exposure concentrations	There was only one treated field and two controls.	**1**
Transparency of data.	Summarized data presented with estimates of variability (SE) and sample sizes. Few raw data presented.	**2**
Number of samples and replication.	The number of samples for the activity data totalled 90,000 foraging flights for >3000 RFID-tagged bees but only one exposure concentration (1 treated field). There were 4 hives per apiary site; three apiary sites per field; 1 treated and 2 control fields.	**1**
Overall evaluation of methods		**1.60**
Score for expert judgment on quality of the study - There was lack of statistical rigor in the experimental design and analyses **(major weakness)**	**0.5**	**0.80**

Response 1. Effects on honeybee activity in the crop		**Score**
Statistical significance of responses	No statistical analyses were applied to the data and no P values were presented. That said, there was no apparent adverse effect on the in-crop foraging activity of bees (Figure 1).	**0**
Concentration- or dose-response	There was only one treated site and two control sites so a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-4. Effects on flight data for tagged bees – foraging lifespan; total no. of flying days per bee; means trip duration; flights per bee per flying day; mean flight duration per bee per flying day; mean flying time per bee all cohorts (h).	**Score**

[42] Pilling E, Campbell P, Coulson M, Ruddle N, Tornier I . 2013. A four-year field program investigating long-term effects of repeated exposure of honey bee colonies to flowering crops treated with thiamethoxam. PLoS One 8:e77193.

Statistical significance of responses	No statistical analyses were applied to the data and no P values were presented. That said, there was no apparent adverse effect on the foraging activity of bees (Table 3; Figure 3; Table 4; Figure 4; Figure 5; Table 5).	**0**
Concentration- or dose-response	There was only one treated site and two control sites so a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

No residues of either TMX or the metabolite clothianidin were detected in any of the samples of plants, flowers, pollen, or nectar collected from the control fields above the level of quantification (limits of quantitation for TMX were 1.0 µg/kg in whole plants, flowers, and pollen and 0.5 µg/kg in nectar; limit of quantitation for clothianidin in all sample matrices was 1.0 µg/kg). Residues of 1.0 µg TMX/kg and 3.0 µg clothianidin/kg were detected in pollen from the treated crop. Nectar from the treated crop contained 1.8 µg TMX/kg and no detectable metabolite.

Exposure estimates determined that honeybee exposure to TMX was 0.14 ng TMX/d. This estimate of exposure was based on the data from the dataloggers and the residues measured. Based on a requirement of 12 mg sugar/h to fly[43] the foraging behavior of the bees suggests that per flight they would expend 6 mg sugar to fuel flight (assuming they spend the entire time flying) and collect/carry 40 mg nectar per load[44] (Winston 1987). In this scenario, based on 1.8 µg TMX/kg nectar the bees collected 0.072 ng TMX per nectar load and consumed 0.036 ng TMX (based on 30% sugar in nectar, assuming all flight is fueled by the collected nectar and the absorption of TMX into the gut is linear with that of the nectar). With a mean of 4 foraging trips/d, this equates to 72 mg nectar/d to fuel flight (just fewer than 2 foraging trips) if all energy was sourced from collected nectar and results in exposure to a total of 0.14 ng TMX/d. In fact, the metabolism of TMX within the bee and the time course of exposure over the course of the day are likely to result in the body burden being far lower.

Expert Judgement		
QA	Yes	April 10, 2016
SEJ	Yes	May 30, 2016

[43] Rortais A, Arnold G, Halm MP, Touffet-Briens F. 2005. Modes of honeybee's exposure to systemic insecticides: Estimated amounts of contaminated pollen and nectar consumed by different categories of bees. Apidologie 36:71–83

[44] Winston M. 1987. The Biology of the Honey Bee. Harvard University Press, Cambridge, MA, USA

Effects of TMX on honeybees resulting from exposures to dust during seeding of seeds treated with TMX

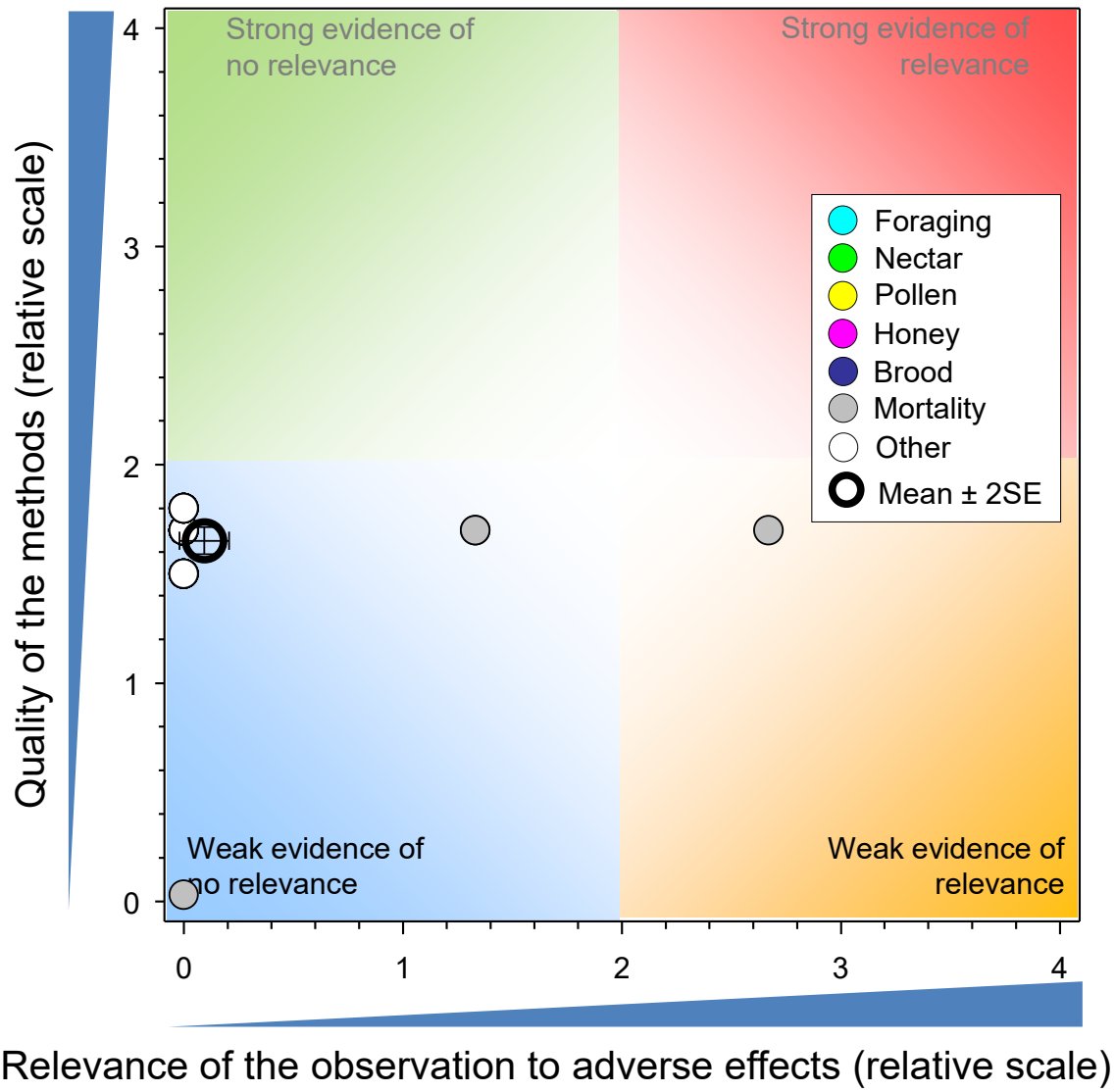
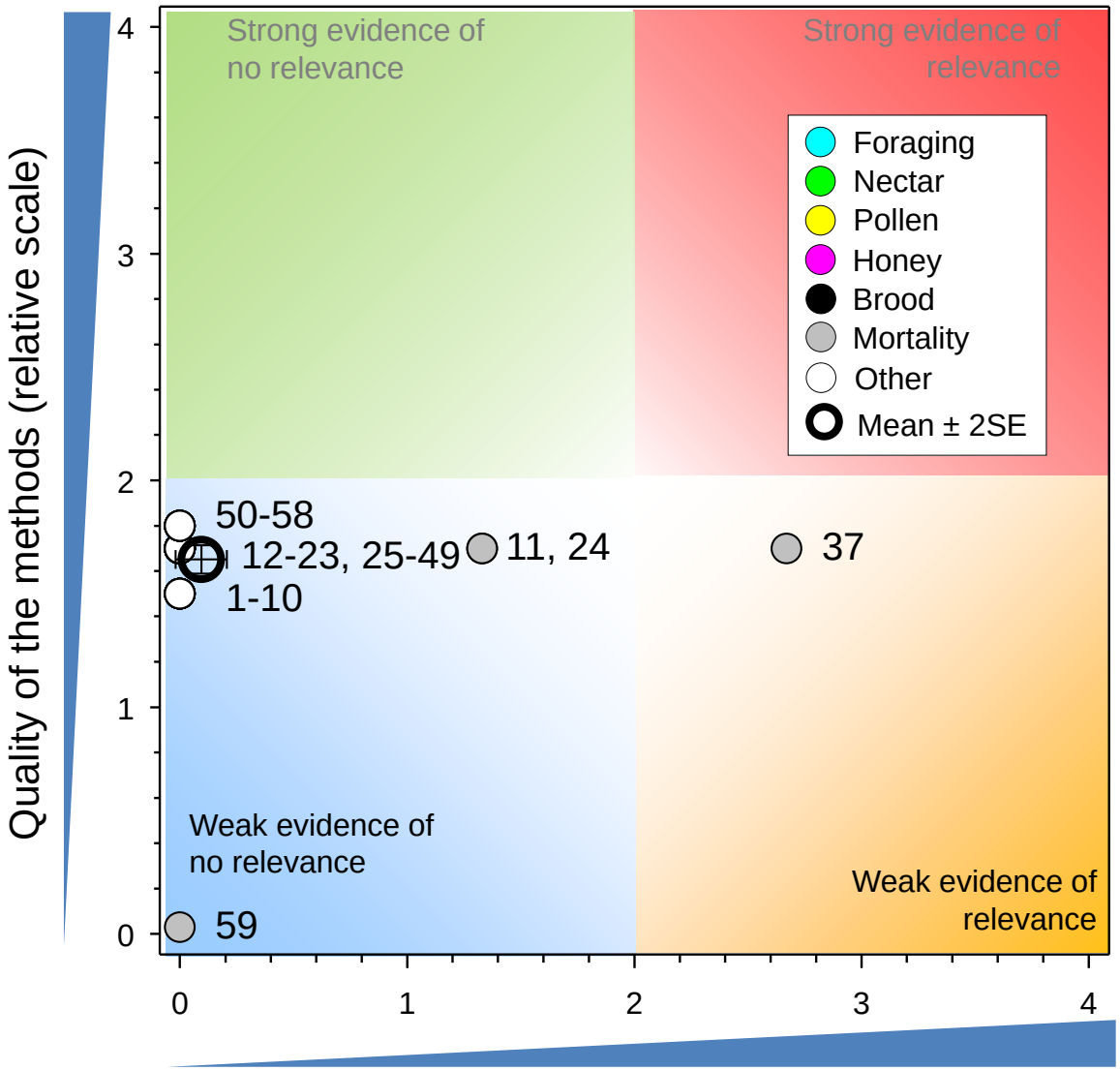


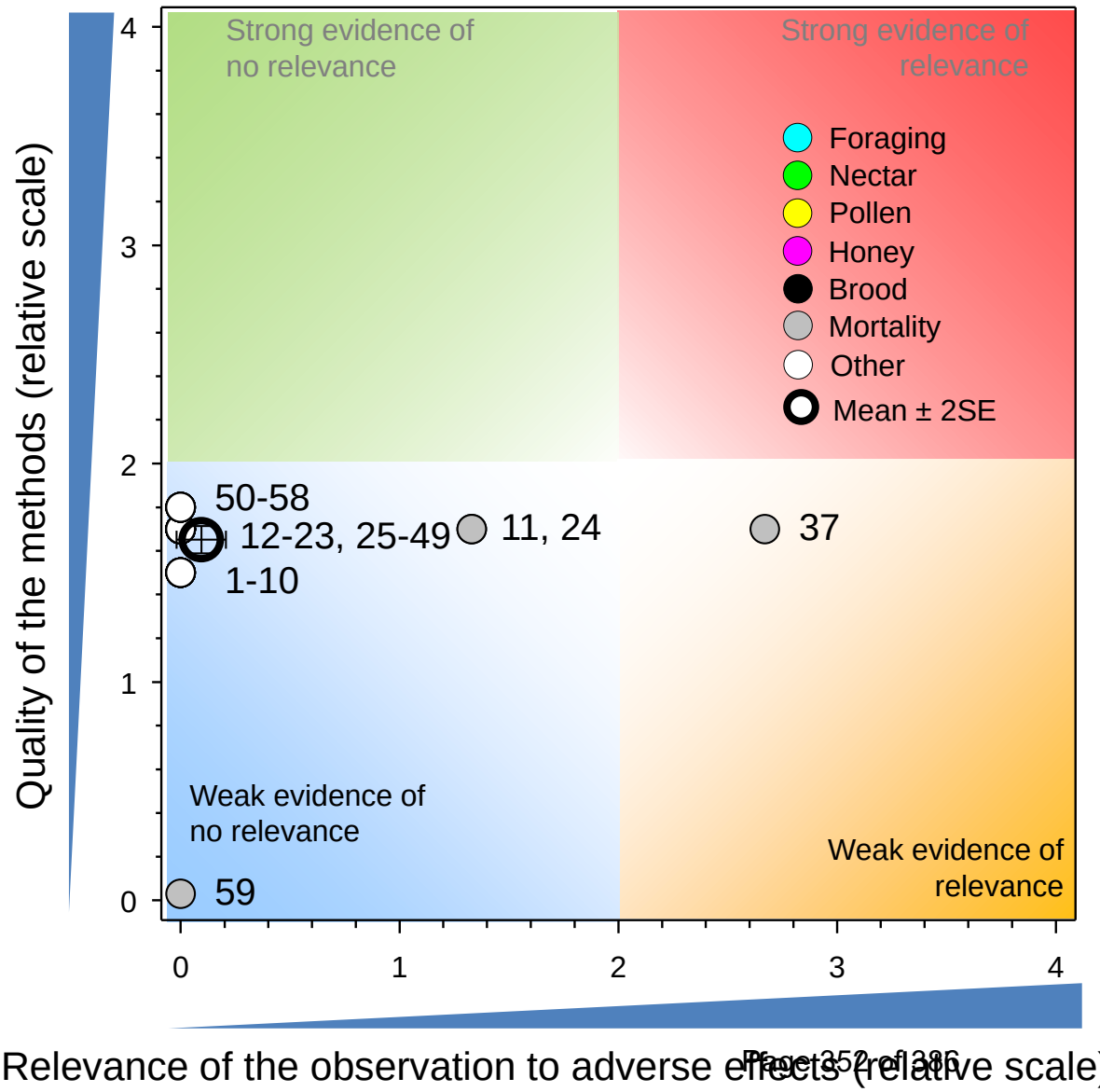
Figure 5. Quality and relevance of effects observed in honeybees exposed in controlled field studies resulting from exposures to dust generated during drilling, n = 59. Symbols may obscure others, see

Effects of TMX on honeybees resulting from exposures to dust during seeding of seeds treated with TMX



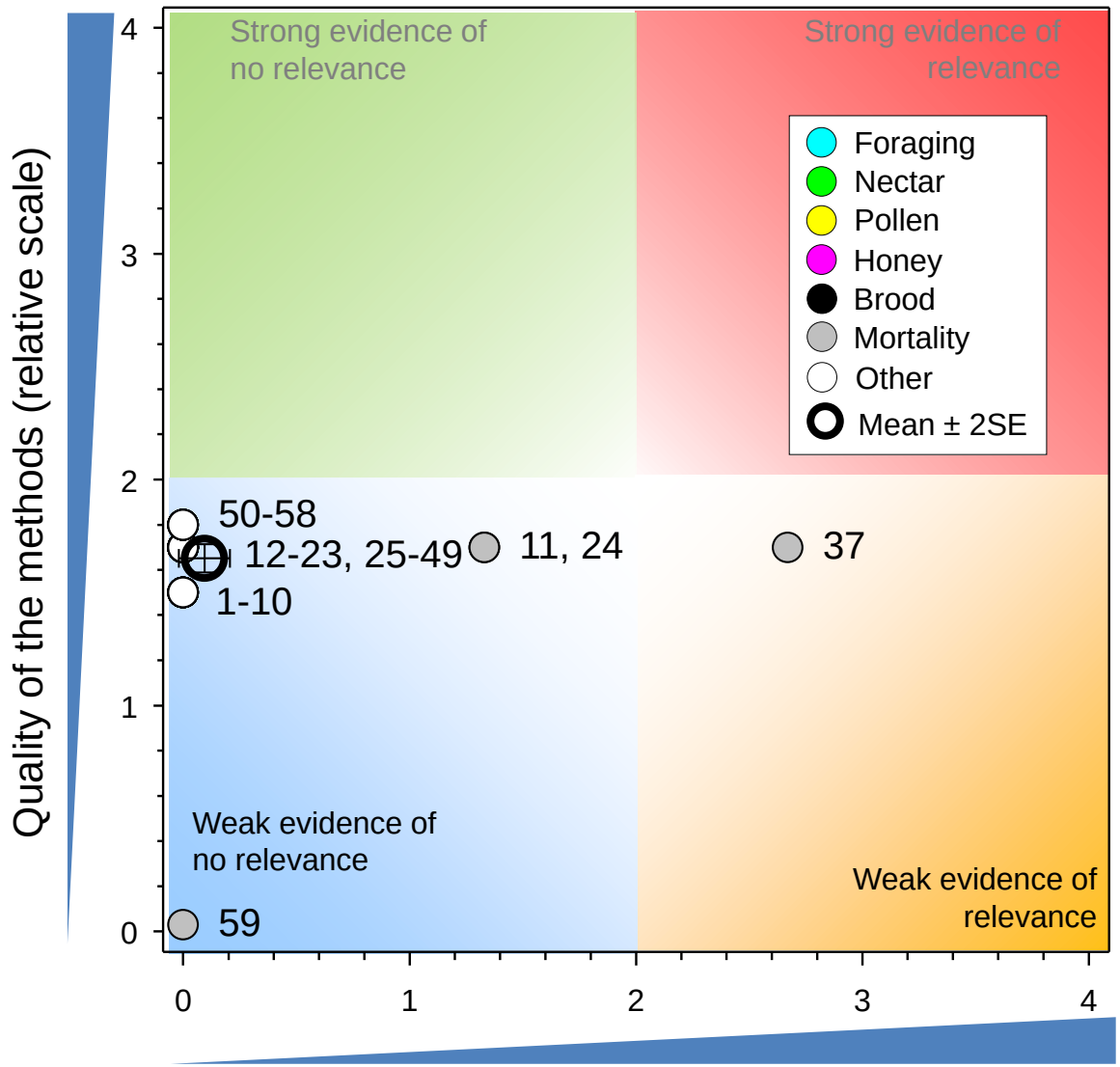
1 = (Syngenta 2010i) Resp 1
2 = (Syngenta 2010i) Resp 2
3 = (Syngenta 2010i) Resp 3
4 = (Syngenta 2010i) Resp 4
5 = (Syngenta 2010i) Resp 5
6 = (Syngenta 2010i) Resp 6
7 = (Syngenta 2010i) Resp 7
8 = (Syngenta 2010i) Resp 8
9 = (Syngenta 2010i) Resp 9
10 = (Syngenta 2010i) Resp 10
11 = (Syngenta 2012d) Resp 1
12 = (Syngenta 2012d) Resp 2
13 = (Syngenta 2012d) Resp 3
14 = (Syngenta 2012d) Resp 4
15 = (Syngenta 2012d) Resp 5
16 = (Syngenta 2012d) Resp 6
17 = (Syngenta 2012d) Resp 7
18 = (Syngenta 2012d) Resp 8
19 = (Syngenta 2012d) Resp 9
20 = (Syngenta 2012d) Resp 10
21 = (Syngenta 2012d) Resp 11
22 = (Syngenta 2012d) Resp 12
23 = (Syngenta 2012d) Resp 13
24 = (Syngenta 2012a) Resp 1
25 = (Syngenta 2012a) Resp 2

Effects of TMX on honeybees resulting from exposures to dust during seeding of seeds treated with TMX



26 = (Syngenta 2012a) Resp 3
27 = (Syngenta 2012a) Resp 4
28 = (Syngenta 2012a) Resp 5
29 = (Syngenta 2012a) Resp 6
30 = (Syngenta 2012a) Resp 7
31 = (Syngenta 2012a) Resp 8
32 = (Syngenta 2012a) Resp 9
33 = (Syngenta 2012a) Resp 10
34 = (Syngenta 2012a) Resp 11
35 = (Syngenta 2012a) Resp 12
36 = (Syngenta 2012a) Resp 13
37 = (Syngenta 2012b) Resp 1
38 = (Syngenta 2012b) Resp 2
39 = (Syngenta 2012b) Resp 3
40 = (Syngenta 2012b) Resp 4
41 = (Syngenta 2012b) Resp 5
42 = (Syngenta 2012b) Resp 6
43 = (Syngenta 2012b) Resp 7
44 = (Syngenta 2012b) Resp 8
45 = (Syngenta 2012b) Resp 9
46 = (Syngenta 2012b) Resp 10
47 = (Syngenta 2012b) Resp 11
48 = (Syngenta 2012b) Resp 12
49 = (Syngenta 2012b) Resp 13
50 = (Syngenta 2013a) Resp 1

Effects of TMX on honeybees resulting from exposures to dust during seeding of seeds treated with TMX



51 = (Syngenta 2013a) Resp 2
52 = (Syngenta 2013a) Resp 3
53 = (Syngenta 2013a) Resp 4
54 = (Syngenta 2013a) Resp 5
55 = (Syngenta 2013a) Resp 6
56 = (Syngenta 2013a) Resp 7
57 = (Syngenta 2013a) Resp 8
58 = (Syngenta 2013a) Resp 9
59 = (Stanley et al. 2015) Resp 1

(Syngenta 2010i)
Report: Syngenta. 2010. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Seeding and Residues in Guttation Liquid, on Honeybee Colonies in Alsace (France) in 2009. Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B_10921 - A9700B. 230 p.

The objective of the study was to determine the effect of residues of thiamethoxam (CGA293343) in dust generated during maize seeding and residues in guttation liquid on honeybee colonies under field conditions following the OEPP/EPPO Guideline No. 170 (2001)[4] with modifications, and with some integration of the IVA Guideline (1992), the EU Directive 91/414/EEC (1997).

Responses 1-10: Quality of methods		Score
Experimental design and hypotheses	The study was carried out at two separate field plots (approximately 1.8 ha in the control and 1.4 ha in the TMX treated field plot; separated by 2.5 km) located near Drusenheim in the region of Alsace, France. On both field plots, maize seed was drilled at approximately 110,000 seeds/ha (target 69.3 g TMX/ha in the treated plot; actual was 78.7 g TMX/ ha). The control (untreated seed) and TMX-treated seed were drilled on May 5 and 6, 2009, respectively (Tables 5 and 6). Application rates were verified by analysis and the loading rates and drill rates summarized on p. 21 (Tables 5 and 6). Six bee colonies were placed at the treated and six at the control field plots. The adjacent crop was winter oilseed rape (wOSR) from which dust samples were collected (see separate WoE) and observations on foraging honeybees were made. Honeybee colonies (n = 6 hives/treatment; healthy queen-right) were placed into the maize field plots (Figures 2 and 3) comprising the TMX and control treatments on April 24, 2009 just before maize seeding and were maintained from seeding for up to 41 days after maize emergence (exposure phase). In the treated field, colonies were positioned within the oilseed rape crop with the hive entrances facing the oilseed rape crop (Figure 4). In the control field hives were positioned on the grass verge at the edge of the field all facing towards the oilseed rape crop (Figure 5). Afterwards the bee colonies were moved on 23 June 2009 and maintained and observed at a monitoring site (Wissembourg), without extensive agricultural crops attractive to bees (monitoring phase), until the end of the bee season (September 3, 2009). Assessments endpoints included: mortality in front of the hive (dead bee traps and linen sheets in front of the hives), foraging activity of the bees and the condition of the colonies (colony Quality, number of combs with brood, presence of healthy queen, food (pollen and nectar) storage; and comb area with brood (eggs, larvae, pupae or capped brood) were assessed before and during the period of seeding and subsequent guttation. Dust generated during maize seeding was collected within the adjacent oilseed rape crop along a distance gradient using Petri dishes (Table 18). After the maize had emerged, honeybee mortality and flight intensity were observed during guttation and samples of guttation fluid were taken and analysed (Table 24). An assessment of brood development was done once shortly before the set-up of the colonies at the fields and at several points during the exposure and monitoring	**3**

	phase (Tables 16-17). The influence of the test item was evaluated by comparing the results in the test item treatment to the control using graphs and tabular data (no statistical analyses). Guttation started after the flowering of wOSR ended. Meteorological data were collected and reported (Tables 5-9). Source of colonies was identified and all were produced at the same time and the queens originated from one breeding line to promote uniformity. The number of bees per colony was estimated according to published methods (Imdorf & Gerig, 1999[2], and Imdorf et al., 1987)[3]. The colonies were as homogeneous as possible at the start of the study. Dead bee traps were fixed to record the number of dead bees carried out of the hives by bees. Soils were characterized (Subsection 4.1, p. 26) and although soil samples were collected, no residues were measured (p. 20). There were no statistical procedures applied to the data and no P or r^2 values provided (***major weakness***). Methods for sample collection and experimental design were either described or cited. Specifications for the test material and details on drilling and crop maintenance provided as well as drilling rates which were verified (Subsection 3.3.6, p. 20; Tables 4-6). Historical pesticide use was reported (Tables 1 and 2, respectively) for both the TMX and control fields. Analytical methods for residue analyses were included and detection and quantitation levels reported. Field fortified samples were also used.	
Use of GLP and QA/QC.	GLP study, signatures, study plan, deviations, amendments, QA audit, certificates etc.	**4**
Exposure concentrations	Single concentration was applied to maize. Residues were measured in dust, plant material, nectar and pollen (see below) of subsequent crops grown on site.	**3**
Transparency of data.	Raw and summary data were provided in the report and appendices.	**4**
Number of samples and replication.	There were two treatments (fields) – one control and one TMX treatment.	**1**
Overall evaluation of methods		**3.00**
Score for expert judgment on quality of the study- There were no statistical procedures applied to the data and no P or r^2 values provided (**major weakness**).	**0.5**	**1.50**

Response 1. Effects on mortality – number of bees in dead bee traps and linen sheets		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. Mean mortality in the TMX-exposed colonies was either consistently higher than or comparable to that in the control colonies prior to exposure (Figure 9; Tables 10 and 11) and throughout the study (except for just after start of exposure where mortality in the control was higher than that in the treatment). The peak in mortality, observed on 13 May 2009 (mean of 58.3 bees/hive/day in the test item treatment), was prior to the first guttation event which was seen on 14 May 2009. The explanation for the high mortality was a brood assessment taking place on 12 May 2009. Later on, mortality remained	**0**

	at a relatively low level in both treatments during the exposure period (< 30 dead bees/hive/day).	
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2. Effects on colony Quality – brood nest size		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. The brood nest size (number of combs containing brood) at the first brood assessment was comparable in both treatment groups and the means were 7.83 combs per colony in the control and 8.17 combs per colony in the treatment group (Figures 7 and 8). At the end of exposure (23 June 2009) a mean of 11.5 combs per colony contained brood in control and 9.17 combs per colony in the treatment group (Tables 16 and 17). The colony Quality remained similar between the two treatments, with the control being slightly stronger than the test item except for the last assessment where the Quality was similar.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 3-5. Effects on colony Quality – brood development (comb area with eggs, larvae and capped brood)		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. Results for the brood assessments are tabulated in Tables 16-17, respectively, for the control and TMX treatments. Figures 7 and 8 show the mean percentage brood area for the control and TMX treatment. The individual hive data are provided in Figures 11 to 22. There were no TMX-related differences apparent from these data and the patters between the two groups were similar.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**

reproduction, and fitness)		
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 6-7. Effects on colony Quality – food storage (nectar & pollen)		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. Figures 7 and 8 show the mean percentage food area (nectar & pollen) for the control and TMX treatments, respectively. The levels of brood and food during the assessment period were very similar with no apparent differences.	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 8-9. Effects on foraging activity & flight intensity of honeybees		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. During the entire 40-day guttation period very low flight intensity was observed within the treated field and, during this period, no honey bees were seen foraging on the guttation droplets despite intensive observations (Tables 12-15).	**0**
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 10. Effects on colony Quality – number of bees/colony		**Score**
Statistical significance of responses	There were no statistical procedures applied to the data and no P or r^2 values provided. Colony Quality (number of bees/colony; Figure 6 - treatment means; Figure and 10 – individual colonies). Colony Qualitys (number of bees) in both treatments showed the same tendency to increase and decrease during the assessment period; however, for the most part colony Quality reflected by the number of honeybees per hive was greater in most control hives during the guttation period and	**0**

	following assessment periods but comparable by the end of the season (September 2009).	
Concentration- or dose-response	A concentration-response was not applicable (NA); only one rate was applied; two fields – control and TMX treatment.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	No mechanism or mode of action was proposed	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative
Honeybee colonies were exposed to TMX in dust generated during drilling and also potentially exposed to residues of TMX in guttation. The presence of TMX residues was confirmed in dust samples taken after drilling of the crop as well as in guttation fluid at ecological relevant concentrations. Despite a background of TMX in the adjacent oilseed rape crop, only one sample of honeybees taken from dead bee traps contained residues of TMX. During the guttation exposure, none of the dead bee samples contained TMX; however, two samples contained CTD.

The colony Quality remained similar between the two treatments, with the control colonies being slightly stronger than those in the TMX treatment, except for the last assessment where the Quality was similar. Mortality remained at a relatively low level (mean of < 30 dead bees/hive/day). During the entire 40-day guttation period, very low flight intensity was observed within the treated field and during this period; no honey bees were seen foraging on the guttation droplets despite intensive observations.

Expert Judgement		
QA	Yes	May 31, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2012f)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Stade, Germany in 2010. Niefern-Öschelbronn, Germany: Syngenta Ltd. (Unpublished Report). Report A9700B_10951. 15 p

And

(Syngenta 2012d)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Stade, Germany in 2010. Final Report Amendment 1. Syngenta Ltd, Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B-S10-01860. 366 p

A GLP study was conducted in the region of Niedersachsen, Germany from May 14, 2010 to July 6, 2011 to determine if dust generated from TMX-treated maize seed has TMX residues sufficiently high to adversely affect honeybees and to determine if guttation fluid from plants grown from treated seed had TMX residues that would adversely affect honeybees. The first report listed above is the executive summary and the second report is the comprehensive GLP study. Exposures in bee-relevant matrices are assessed in the corresponding WoE_{EXP}.

Responses 1-13: Quality of methods		Score
Experimental design and hypotheses	The objective of this study was to determine the effects of residues of TMX (CGA293343) in dust generated during maize seeding and residues in guttation liquid on honeybee colonies under field conditions. The bee colony observation period extended from 14 May 2010 to 29 March 2011. Maize (var. NK Falkone), treated with the seed treatment (0.69 mg a.s. TMX/seed) and fungicide control (0.91 g a.s. metalaxyl-M/100 kg seed + 2.55 g a.s. fludioxonil/100 kg seed) and an untreated control (untreated with neonicotinoid insecticides) were sown in fields near Stade in the region of Niedersachsen, Germany, on 18 May 2010 (nominal seeding rate 34.32 kg/ha, approximately 110,000 seeds/ha). The actual seeding rate for the TMX-treated field was 111,026 seeds/ha (equivalent to 34.64 kg seeds/ha), resulting in an application rate of 76.6 g TMX/ha. The TMX field measured 1.75 ha; the size of the control field was 1.53 ha. The two maize fields (TMX and Control, respectively) were in Bremervörde and Hechthausen, near Stade and were separated by 12 km. The pesticide history for each field was provided (Tables 47-50). Meteorological records were provided (Tables 24-26). Soil characterization was provided as well as shipping and storage conditions for samples (Table 53). Critical dates for sampling and assessing were summarized (Tables 6-7). Flowering stages were monitored and reported (Tables 27). Six bee hives of comparable Quality (10,200 to 17,400 bees per hive) were placed at the TMX-treated field plots (T1 to T6) and six at the control field plots (C1 to C6). Each hive comprised two boxes and 24 individual combs. Honeybees were maintained on the maize field plots four days before maize drilling until the end of the crop flowering period.	**4**

	Beginning with the emergence of maize seedlings (exposure phase I, BBCH 10, 31 May 2010), bee mortality, occurrence of guttation, bee activity and the behaviour of the bees were assessed for 41 days (until 10 July 2010). Exposure phase II was defined as the period from the end of guttation (42 days after seedling emergence, 12 July 2010) to the onset of flowering (28 July 2010 (T), 30 July 2010 (C)). During this period, only regular brood assessments were conducted. For the period of flowering (exposure phase III, BBCH 53-65, 29 July (T) and 1 August (C) to 16 August 2010), mortality, flight intensity and behaviour of the bees were recorded. Hives were equipped with dead bee traps and linen sheets were laid down in the crop to assess dead bees in the field. Pollen samples from pollen traps were collected on three sampling dates for identification. Samples of guttation liquid, soil, maize plants, pollen taken directly from maize plants and forager bees, and dead bees from dead bee traps were collected for residue analysis. In addition, bee and nectar samples were taken on specific occasions to conduct bee disease and virus analysis. After the end of the crop flowering period, the bee hives were transported to an isolated monitoring location (Himmelpforten, Lower Saxony region, 16 August 2010), for further brood assessments and overwintering. Here colony health and Quality as well as brood development were assessed once, 11 days after their arrival at the monitoring site (27 August 2010) and then every three weeks until the end of bee season (7 October 2010). No invasive assessments were carried out while colonies were overwintering (between October 2010 and March 2011). The last brood assessment was conducted on 29 March 2011 to determine the overwintering success. Colony health and Quality and brood development were assessed regularly over the whole year except for the overwintering period (between October and March). The experimental phase started in 2010 (14 May 2010) with the first brood assessment before installation of the bee hives and ended with the end of bee disease analysis in 2011 (6 July 2011). Methods followed those recommended in OEPP/EPPO Guideline No. 170 (3) (2001)[4], with modifications; and Commission Directive 96/68/EC (amending Council Directive 91/414/EEC). The start of bee exposure to the test item treated maize, more precisely to the dust generated during drilling is defined as DAD 0 (DAD = Days after drilling of maize). The period beginning with the emergence of the maize plants associated with the appearance of guttation droplets is defined as DAE 0 (DAE = Days after start of emergence of the maize seedlings) and the start of the flowering period is defined as DAF 0 (DAF = Days after start of flowering). Statistical analyses of data did not occur and no P values or r^2 values were included. Comparisons between treatments were made using professional judgement (***major weakness***).	
Use of GLP and QA/QC.	GLP study – comprehensive; study plan and deviations, certificates, QA and signatures	**4**
Exposure concentrations	There was only one treatment field and one application rate so no exposure concentration gradient. Analytical chemistry followed GLP and methods were acceptable as were LODs and LOQs. Residues were measured in guttation fluid and in pollen. However, TMX residues in the	**4**

	control samples was a potential weakness. Seed loading was verified (Table 1).	
Transparency of data.	Raw and summary data provided.	**4**
Number of samples and replication.	Repeated metrics measured over time on pseudo-replicates as there were only two fields: a TMX treatment and a control. Sample sizes were adequate.	**1**
Overall evaluation of methods		**3.40**
Score for expert judgment on quality of the study- TMX residues in the control samples constituted a potential weakness; a labelling mix up was suspected but not proven; no statistical procedures were applied to the data and no P or r^2 values were provided (***major weakness***)	**0.5**	**1.70**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. Comparisons to the results for the control treatment were made. The mean number of dead bees/hive/day was comparable between treatments (Figures 1 and 6) and consistently higher in the TMX treatment relative to the control (Table 10.4.3, p. 8 of[45] or p. 56 of[46]) between 2 and 16 days after drilling. No dead bees were found on the linen sheets in both treatments during the exposure phase 3. Data were provided for the exposure phase 1 and phase 3 in Tables 8-9 and 10-11, respectively.	**4**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Although there were several days when mortality in the TMX treatment was greater than that in the control treatment, over the three phases (pre-exposure, exposure, and post-exposure), the mortality rates were similar between treatments (Table 10.4.3, p. 8 of[45] or p. 56 of[46]).	**0**
Mechanism and or mode of action of effect explained	No mechanism was proposed.	**0**
Overall evaluation of relevance (computed)		**1.33**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on honeybee foraging activity & flight intensity		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. Mean flight intensity was comparable between treatments on days 0-13 after flowering (e.g., 32.6 and 31.6 forage bees/30 plants/min for TMX and control treatments, respectively)	**0**

[45] Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Stade, Germany in 2010. Niefern-Öschelbronn, Germany: Syngenta Ltd. (Unpublished Report). Report A9700B_10951. 15 p

[46] Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Stade, Germany in 2010. Final Report Amendment 1. Syngenta Ltd, Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B-S10-01860. 366 p

	(Tables 12-13). Foraging activity data is provided in Figure 2; Tables 22-23.	
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	No apparent adverse effects on flight intensity attributable to TMX were observed in the test item field compared to the control.	**0**
Mechanism and or mode of action of effect explained	Differences in flight intensity in the test fields recorded on single occasions were caused by different biological conditions at the field sites rather than the treatment in the test fields.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. No behavioural differences of the bees in the TMX treatment group were observed during the exposure periods I to III compared to the bees in the control group (Tables 14 and 15). No abnormal behaviour was observed in the test item field. On DAF 5 bees showing intensive flying behaviour without landing on the crop were noticed in the off-crop area in the control field.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-6. Effects on colony Quality – number of bees & brood nest size		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. However, no test item related difference in Quality, as reflected by number of bees (Figures 3 and 7) and brood nest size of the colonies in the TMX treatment compared to the control colonies was observed during the experimental phase of the study from May 2010 until 29 March 2011 (Tables 16 and 17 for assessments; Tables 18-19 for bee keeper checks).	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**

Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7-11. Effects on colony Quality – brood development (eggs, larvae, capped cells) & food stores (honey & pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The brood development (eggs, larvae, capped cells) and food stores (honey and pollen) showed approximately the same tendency to increase or decrease over the observation period from spring to autumn 2010 (Figures 4-5 and Figures 8-19). In spring 2010 all colonies were increasing their breeding activity and had a good food supply from flowering plants. The amount of food stores on the hive combs increased correspondingly. However, no test item related difference in Quality, breeding activity and survival of the colonies in the test item treatment compared to the control colonies was observed during the experimental phase of the study from May 2010 until 29 March 2011.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 12. Effects on colony Quality – overwintering		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. However, no test item related difference in survival of the colonies in the TMX treatment compared to the control colonies was observed during the experimental phase of the study from 14 May 2010 until 29 March 2011. One test item treated colony (T2; Figure 9) was not successful in overwintering.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance to the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	Before overwintering a high *Varroa* mite infestation was detected in colony T2, which probably lead to the colony breakdown during the winter.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 13. Effects on colony health – pests, disease and parasites		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. In general colonies of the control and the test item treatment were in a good health condition. No spores of *Paenibacillus larvae*, *Malpighamoeba mellificae* and no *Acarapis woodi* mites were found in any of the samples taken in 2010 and 2011 (Appendices 1 and 2).	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse response was discernable from these data, the relevance of the effects could not be ascertained.	**0**
Mechanism and or mode of action of effect explained	Since no significant adverse response was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

No honeybee was observed collecting or taking up guttation droplets from maize plants in the test item treatment field during the whole time of guttation observation. Overall, in the test item treatment field more bees were observed in all five assessment areas in the off-crop area compared with the control plot.

Expert Judgement		
QA	Yes	May 31, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2012g)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Alsace, France in 2010. Niefern-Öschelbronn, Germany: Syngenta Ltd. (Unpublished Report). Report A9700B_10952. 14 p

And

(Syngenta 2012a)
Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Alsace, France in 2010. Final Report Amendment 1. Syngenta Ltd, Bracknell, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B S10-01857. 346 p

A GLP study was conducted in the region of Alsace, France from May 5, 2010 to July 4, 2011 to determine if dust generated from TMX-treated maize seed has TMX residues sufficiently high to adversely affect honeybees and to determine if guttation fluid from plants grown from treated seed had TMX residues that would adversely affect honeybees. The first report listed above is the executive summary and the second report is the comprehensive GLP study. Exposures in bee-relevant matrices are assessed in the corresponding $WoE_{EXP.}$

Responses 1-13: Quality of methods		Score
Experimental design and hypotheses	The objective of this study was to determine the effects of residues of TMX (CGA293343) in dust generated during maize seeding and residues in guttation liquid on honeybee colonies under field conditions. The bee colony observation period extended from 5 May 2010 to 21 March 2011. Maize (var. NK Perform), treated with the seed treatment (0.68 mg a.s. TMX/seed) and fungicide control (1.12 g a.s. metalaxyl-M/100 kg seed + 2.54 g a.s. fludioxonil/100 kg seed) and an untreated control (untreated with neonicotinoid insecticides) were sown in the region Alsace, France, on 17 May 2010 (control seeding rate 29.59 kg/ha, approximately 103,825 seeds/ha). The seeding rate for the TMX-treated field was 101,684 seeds/ha (equivalent to 28.98 kg seeds/ha), resulting in an application rate of 69.15 g TMX/ha. The TMX-treated field was located near La Petite Pierre and the control field was near Puberg. The TMX field measured 1.97 ha; the size of the control field was 2.38 ha. The two field plots were separated by 4.75 km. Six bee hives were placed at the TMX-treated field plots (T1 to T6) and six at the control field plots (C1 to C6) within 7 and 3 m of the fields, respectively. Each colony had one queen and ~5000 to 11,500 bees, with two boxes and 20 individual combs. Honeybees were maintained on the maize field plots for 11 days before maize drilling until the end of the crop flowering period. During the first exposure phase (I), starting with the emergence of maize seedlings; bee mortality, occurrence of guttation, bee activity and the behaviour of the bees were assessed for 41 d (until 8 July 2010). Exposure phase II was defined as the period from the end of guttation (42 days after seedling emergence, 10 July 2010) to the onset of flowering (25 July 2010). During this period only	**4**

	regular brood assessments were conducted. For the period of flowering (exposure phase III, BBCH 59-69, 26 July 2010 to 4 August 2010) mortality, flight intensity and behaviour of the bees were recorded. The exposure period lasted ~ 41 d. After the end of flowering, the bee hives of both treatment groups were transported to an isolated monitoring location (Haguenau in the region of Alsace, France), for overwintering assessment and monitored until 21 March 2011. Dates for phases were provided in subsection 3.4.2. The pesticide use history of all field sites selected for this study was known for the two previous cropping seasons and earlier (Tables 48-53). Meteorological data were collected and reported (Tables 26-28). Soil samples were collected for residues analyses and characterized (Tables 36 & 41). Storage and shipping of samples destined for residue analyses were described (Table 55). Flowering was monitored as was guttation in plants. Diseases were monitored in samples (see subsection 3.5.3.4 and Table 9). Hives were equipped with dead bee traps and linen sheets were laid down in the crop to assess dead bees in the field; methods and procedures were described in detail. Mortality was measured in front of the bee hives and samples of dead bees were collected for residue analyses. Mortality was also measured in the field. Condition of the colonies and brood development was assessed before the hives were installed at the site and thereafter at regular intervals using brood assessment procedures and beekeeper checks (subsection 3.5.1.4 and 3.5.3.4). Flight intensity and activity were assessed on several occasions both in front of the hives and in the fields (subsection 3.5.3.2). Bee disease and virus analyses were described (Appendices 1-2). Samples of soil, pollen from plants and forager bees, maize plants, dead bees and guttation liquid were analysed at appropriate intervals for residues of TMX and CTD. Pollen samples from pollen traps were collected on three sampling dates (3, 5 and 7 days after flowering) for identification. Samples of guttation liquid (during flowering), soil (before planting), pollen taken directly from maize plants and forager bees, and dead bees from dead bee traps were collected for residue analysis (Appendix 3). In addition, bee and nectar samples were taken on specific occasions to conduct bee disease and virus analysis. After the end of the crop flowering period, the bee hives were transported to an isolated monitoring location (Haugenau), August 4, 2010), for further brood assessments and overwintering. Here colony health and Quality as well as brood development were assessed once, 8 days after their arrival at the monitoring site and then every three weeks until the end of bee season (15 October 2010). No invasive assessments were carried out while colonies were overwintering (between October 2010 and March 2011). The last brood assessment was conducted on March 21, 2011 to determine the overwintering success. Methods followed those recommended in OEPP/EPPO Guideline No. 170 (3) (2001)[4], with modifications; and Commission Directive 96/68/EC (amending Council Directive 91/414/EEC). Methods were described in detail. The start of bee exposure to the test item treated maize, more precisely to the dust generated during drilling is defined as DAD 0 (DAD = Days after drilling of maize). The period beginning with the emergence of the maize plants associated with the appearance of guttation droplets is	

	defined as DAE 0 (DAE = Days after start of emergence of the maize seedlings) and the start of the flowering period is defined as DAF 0 (DAF = Days after start of flowering). Statistical analyses of data did not occur and no P values or r^2 values were included. Comparisons between treatments were made using professional judgement (**major weakness**).	
Use of GLP and QA/QC.	GLP study with comprehensive documentation.	**4**
Exposure concentrations	There was only one treatment field and one application rate so no exposure concentration gradient. Analytical chemistry followed GLP and methods were acceptable as were LODs and LOQs. Residues were measured in guttation fluid and in pollen. Seed dressing was verified (subsection 3.1); drilling rates were measured.	**4**
Transparency of data.	Summary and raw data were comprehensive	**4**
Number of samples and replication.	Repeated metrics measured over time on pseudo-replicates as there were only two fields: a TMX treatment and one control. Sample sizes were adequate.	**1**
Overall evaluation of methods		**3.40**
Score for expert judgment on quality of the study- no statistical analyses of effects data was a major weakness	**0.5**	**1.70**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. Comparison to the results for the control treatment were made. The daily mean number of dead bees (worker bees + pupae + young bees) in front of the hives (dead bee traps and linen sheet) during the time of exposure phase I was 16.9 dead bees/hive in the TMX-treated group compared to 11.0 dead bees/hive in the control group. During exposure phase III, the daily mean number of dead bees was 14.1 dead bees/hive in the test item treated group compared to 7.9 dead bees/hive in the control group. During exposure phase II, on DAD 12 to 21 (maximum three out of six hives), DAD 43 (T2) and DAD 72 to 73 (T6) the mean number of dead bees in the TMX treatment was higher compared to the control, but the increase occurred only in single colonies of the test item treatment group, whereas the mortality of the other colonies was in the same range as that recorded in the control colonies. One day (DAD 11) before start of the guttation assessments and once during guttation assessments (DAD 16 = DAE 4) an increased number of dead bees was recorded in four out of six colonies of the test item treatment group compared to the colonies of the control group (DAD 11: T2, T3, T4, T6 and DAD 16: T1, T2, T6). This resulted in a mean number of dead bees of 87.5 dead bees/hive on DAD 11 and 59.0 dead bees/hive on DAD 16 in the test item group compared to 15.3 and 18.2 dead bees/hive in the control group on the corresponding assessment days (Figures 1 and 6; Tables10-13). When considering the entire assessment period, TMX had no overall effects on honeybee mortality, with comparable levels and periods of mortality observed between both treated and control plot hives.	**4**

Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	There were only 32 of 384 observations when dead bee trap mortality for individual hives was ≥40 dead bees per hive. Of these 32 instances, 12 occurred prior to seed drilling. For the hives in the control treatment, there were 15 of 384 occasions when bee mortality was ≥40 dead bees per individual hive, ten of which occurred prior to seed drilling. No TMX or CTD residues were detected above the level of quantification in control field bee samples.	**0**
Mechanism and or mode of action of effect explained	No mechanism was proposed or discussed.	**0**
Overall evaluation of relevance (computed)		**1.33**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on honeybee foraging activity & intensity		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The mean flight intensity in the TMX-treated field was slightly lower or approximately comparable to the flight intensity in the control field (Figure 2; Tables 14-15). During the first 4 days of assessments the number of forager bees observed in the two test fields was generally low. From DAF 4 to DAF 6 bees were recorded foraging on the flowering maize plants with flight intensity in the test item field lower than in the control field; e.g., TMX treatment: 3.4 to 20.0 bees/30 plants/minute; control treatment: 14.0 to 23.4 bees/30 plants/minute. The mean flight intensity during time of exposure was 44.2 in the test item treated group and 63.0 in the control group. No test item related differences regarding bee flight intensity were observed in the test item field compared to the control.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Differences in flight intensity in the test fields recorded on single occasions were likely to have been caused by different field conditions, such as microclimate and topography, between the treatment and control sites as opposed to any treatment related affects.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. Behavioural observations were normal for all assessments when compared with the control. No behavioural differences of the bees in the TMX treatment group were observed during the entire exposure period to the crop compared to the bees in the control group (Tables 16-17).	**0**

Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects to apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no apparent effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-6. Effects on colony Quality – number of bees & brood nest size		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The pattern for both treatments was similar and the mean number of bees in the hives increased and decreased from the middle of May 2010 up to the last assessment on 15 October 2010 (Figures 3 and 7; Tables 18-19; Tables 21 and 21 for bee keeper checks). At start of the test in May the colonies were of comparable Quality (TMX treatment: 4880 to 11506 bees per colony; Control: 6130 to 10756 bees per colony). All colonies were increasing in size and Quality during spring. In particular colony C5 and C6 of the control group showed a marked increase in the number of bees from the first assessment in May up to the assessment on the 28 June 2010.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7-11. Effects on colony Quality – brood dev't (eggs, larvae, capped cells) & food stores (honey & pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The mean percentage comb coverage of brood (eggs, larvae and pupae) and food (nectar and pollen) in the colonies showed approximately the same development in the control and the treatment group in 2010 (Figures 4-5 and 8-19; Tables 18-19). No test item related difference in Quality, breeding activity and survival of the colonies in the test item treatment compared to the control colonies was observed during the experimental phase of the study from spring 2010 up to end of overwintering in 2010/2011. The honeybee colony development, measured by a comprehensive and thorough observation that recorded hive Quality, brood and food development, overwintering success and colony health was comparable between the treated and untreated control groups.	**0**

Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 12. Effects on colony Quality – overwintering		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. All colonies except T6 and C6 had survived the overwintering and were in good condition. Before overwintering, a high infestation with *Nosema* in hive T6 and in the colony C6 a high *Varroa* mite infestation were detected, which probably lead to their colony breakdown during the winter. Mean colony Quality after overwintering in the treatment group was 9082 bees and 8659 bees in the control group. The ratio of mean colony Quality after compared with before overwintering was approximately the same in the test item group (0.68) and in the control (0.69), which means that the colonies in the test item group and in the control decreased in Quality to the same extent. The overwintering success and Quality after overwintering of the treatment group colonies was not adversely affected by the exposure to TMX seed-treated maize.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect, was observed, no mechanism was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 13. Effects on colony health – pests, disease and parasites		**Score**
Statistical significance of responses)	No statistical procedures were applied to the data and no P or r^2 values were reported. CBPV, KBV, and SBV were not detected in any of the samples taken in 2010 and 2011. DWV was detected in one control sample (C6) and ABPV was detected in two samples of the test item group (T4 and T5) at the start of overwintering (Appendices 1-2). However, since these colonies were in a good health condition after overwintering, it can be concluded, that virus infection did not have a significant effect on bee health during the study. Honey bee disease and virus analysis shows there was no difference in the health condition observed between control and test item colonies during the sampling period 2010-2011.	**0**

Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Expert Judgement		
QA	Yes	May 31, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2012h)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Lorraine (France) in 2010. Niefern-Öschelbronn, Germany: Syngenta Ltd. (Unpublished Report). Report A9700B_10953. 15 p

And

(Syngenta 2012b)
Report: Syngenta. 2012. Thiamethoxam FS (A9700B) - A Field Study with Treated Maize Seeds, Investigating the Effects of Residues from Dust during Drilling, Residues in Guttation Liquid and Flowering Maize, on the Honeybee (*Apis mellifera* L.) in Lorraine, France in 2010. Final Report Amendment 2. Syngenta Ltd, Bracknell, United Kingdom: Syngenta Ltd. (Unpublished Report). Report A9700B S10-01859. 340 p

A GLP study was conducted in the region of Lorraine, France from May 3, 2010 to July 6, 2011 to determine if dust generated from TMX-treated maize seed has TMX residues sufficiently high to adversely affect honeybees and to determine if guttation fluid from plants grown from treated seed had TMX residues that would adversely affect honeybees. The first report listed above is the executive summary and the second report is the comprehensive GLP study. Exposures in bee-relevant matrices are assessed in the corresponding WoE_{EXP}.

Responses 1-13: Quality of methods		Score
Experimental design and hypotheses	The objective of this study was to determine the effects of residues of TMX in dust generated during maize seeding and residues in guttation liquid on honeybee colonies under field conditions. The bee colony observation period extended from May 5, 2010 to March 25, 2011. Maize (var. NK Perform), treated with the TMX treatment (0.68 mg a.s. TMX/seed) and a fungicide mixture (1.12 g a.s. metalaxyl-M/100 kg seed + 2.54 g a.s. fludioxonil/100 kg seed) and an untreated control (untreated with neonicotinoid insecticides) was sown with a Monosem pneumatic single-seed drill with defector, in the region of Lorraine, France, on 18 May 2010. For the control treatment, the seeding rate was 29.17 kg/ha equivalent to 102,349 seeds/ha) (Tables 3-5). For the TMX field, the actual seeding rate was 109,845 seeds/ha, resulting in an application rate of 74.70 g TMX/ha. The amount of dust estimated was 2 g dust/100 kg seeds using Heubach method. The TMX-treatment field measured 3.21 ha; the size of the control field was 1.92 ha. The two field plots were separated by 2.78 km. A second drilling in the control field was required (var. Gazelle) on June 4, 2010. The drilling rate was 35.37 kg seeds/ha (equivalent to 124,542 seeds/ha). Because of the second drilling the flowering of the control plot took longer and the bee hives remained 14 days longer than originally scheduled. The pesticide use history of all field sites selected for this study was known for the two previous cropping seasons. No neonicotinoid insecticides or seed treatments were used in the field plots in at least the previous cropping season before use (Tables 44 to 47). Meteorological data were collected and reported (Tables 24-26). Soil samples were collected for characterisation (Table 37) and residues analyses (Table 32).	**4**

	Six bee hives were placed at (within 4.5 or 5 m, respectively) the TMX-treated field plots (T1 to T6) and six at the control field plots (C1 to C6). Each colony had one queen and 8300 to 15,300 bees, with two boxes each with 10 individual combs. Honeybees were maintained on the maize field plots for 11 days before maize drilling until the end of the crop flowering period. During the first exposure phase (I), starting with the emergence of maize seedlings (June 1, 2010); bee mortality, occurrence of guttation, bee activity and the behaviour of the bees were assessed for 41 days (until July11, 2010). Exposure phase II was defined as the period from the end of guttation (42 days after seedling emergence) to the onset of flowering (27 July 2010). During this period only regular brood assessments were conducted. For the period of flowering (exposure phase III, BBCH 59-69, 28 July 2010 to 4 August 2010), mortality, flight intensity and behaviour of the bees were recorded. The exposure period lasted ~ 41 days. After the end of flowering, the bee hives of both treatment groups were transported to an isolated monitoring location (Haguenau in the region of Alsace, France), for overwintering assessment and monitored until 25 March 2011. Hives were equipped with dead bee traps and linen sheets were laid down in the crop to assess dead bees in the field. Methods were described well for all endpoints measured. Mortality – 3.5.1.3; Colony condition and brood development and disease monitoring - 3.5.1.4; flower development and guttation timing and occurrences3.5.1.5/3.5.1.6; flight intensity – 3.5.3.2; and honeybee behaviour in front of hive-3.5.3.3. Samples of soil (before drilling), pollen from plants and forager bees, maize plants, dead bees and guttation liquid were analysed at appropriate intervals for residues of TMX and CTD. Critical dates were provided (Tables 8-9). Pollen samples from pollen traps and from plants were collected for identification (subsection 3.5.3.7). In addition, bee and nectar samples were taken on specific occasions to conduct bee disease and virus analysis. After the end of the crop flowering period, the bee hives were transported to an isolated monitoring location (August 18, 2010), for further brood assessments and overwintering. Here colony health and Quality as well as brood development were assessed once, 12 d after their arrival at the monitoring site and then every three weeks until the end of bee season (12 October 2010). No invasive assessments were carried out while colonies were overwintering (between October 2010 and March 2011). The last brood assessment was conducted on 25 March 2011 to determine the overwintering success. Methods followed those recommended in OEPP/EPPO Guideline No. 170 (3) (2001)[4], with modifications; and Commission Directive 96/68/EC (amending Council Directive 91/414/EEC). The start of bee exposure to the test item treated maize, more precisely to the dust generated during drilling is defined as DAD 0 (DAD = Days after drilling of maize). The period beginning with the emergence of the maize plants associated with the appearance of guttation droplets is defined as DAE 0 (DAE = Days after start of emergence of the maize seedlings) and the start of the flowering period is defined as DAF 0 (DAF = Days after start of flowering). Statistical analyses of data did not occur and no P values or r^2 values were included. Comparisons between treatments were made using professional judgement (**major weakness**).	

Use of GLP and QA/QC.	GLP study with QA provided; certificates of compliance were included; signature pages. Study plan, deviations and amendments included.	**4**
Exposure concentrations	There was only one treatment field and one application rate so no exposure concentration gradient. Analytical chemistry followed GLP and methods were acceptable as were LODs and LOQs. Residues were measured in guttation fluid and in pollen.	**4**
Transparency of data.	Summary and raw data included and comprehensive	**4**
Number of samples and replication.	Repeated metrics measured over time on pseudo-replicates as there were only two fields: a TMX treatment and a control. Sample sizes were adequate.	**1**
Overall evaluation of methods		**3.40**
Score for expert judgment on quality of the study- no statistical procedures were applied to the data and no P or r^2 values were provided (**major weakness**)	**0.5**	**1.70**

Response 1. Effects on honeybee mortality		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. Comparison to the results for the control treatment were made. Mean mortality per hive on days after drilling (DAD) 2 to 4 of the test item treatment group was 50.8, 67.0 and 75.8 dead bees/hive compared with 5.8, 15.0 and 20.7 dead/bees/hive for the dates in the control treatment group. On DAD 11 and DAD 12 the mean mortality of the test item treatment group was 45.5 and 50.8 dead bees/hive compared with 11.8 and 5.0 dead/bees/hive in the control treatment group. Additionally, on DAD 14 to 16, the specific mean mortality of the test item treatment group was 56.2, 259.3 and 205.0 dead bees/hive compared with 8.5, 25.7 and 8.7 dead bees /hive for the corresponding dates in the control treatment (Figures 1 and 6; Tables 10-13). On the linen sheets spread out in the test fields (mortality within the crop area) no dead bees were found during the exposure phase III (period of flowering) at both test fields.	**4**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Although there were several days when mortality in the TMX treatment was greater than that in the control treatment, over the three phases (pre-exposure, exposure, and post-exposure), the mortality rates were comparable between treatments. On 9 of 41 days, there was an increased number of dead bees in the TMX-exposed colonies relative to that in the controls with significant mortality between 14 and 16 DAD. On 49 of 396 occasions, mortality was >40 dead bees per hive for the TMX treatment; the equivalent for the control treatment was 6 of 396 occasions.	**4**
Mechanism and or mode of action of effect explained	No mechanism was proposed or discussed.	**0**
Overall evaluation of relevance (computed)		
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on honeybee foraging activity & intensity	**Score**

Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The mean flight intensity in the test item treated field during exposure phase III (DAF 0 to DAF 7; DAF = Days After Flowering) was 26.4 forager bees/30 plants/minute over the assessment period (Table 14). However, because of delayed flowering in the control field an evaluation of the flight intensity during exposure of the bee colonies to the flowering maize fields was not possible. Therefore, the flight intensity observed in the test item field could not be compared to the control.	**NA**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	No comparison was possible.	**NA**
Mechanism and or mode of action of effect explained	No comparison was possible	**NA**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4. Effects on honeybee behaviour		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. In general, no behavioural differences of the bees in the TMX-treatment group were observed during the exposure phase I compared to the bees in the control group and no abnormal behaviour was observed in the test item treatment group during the exposure phase III (Table 15). However, on several assessments on DAE 0 to 5, DAE 22 and DAE 32 in the TMX-treated field and DAE 3, DAE 6, DAE 18, DAE 21, DAE 22 and DAE 32 in the control field, single bees were observed showing uncoordinated movements and/or intensive cleaning behaviour (p. 23).	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 5-6. Effects on colony Quality – number of bees & brood nest size		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The daily mean number of dead bees (worker bees + pupae + young bees) in front of the hives during the time of exposure phase I was 25.7 dead bees/hive in the test item treatment group compared to and 9.6 dead bees/hive in the control group. During exposure phase III, the daily mean number of dead bees was 7.4 dead	**0**

	bees/hive in the test item treatment group and 2.4 dead bees/hive in the control group. The mean Quality of the colonies (number of bees in the hives) showed approximately the same tendency to increase and decrease from the middle of May 2010 up to the last assessment before overwintering on 12 October 2010 (Figures 3 and 7; Tables 16-17). At start of the test in May the colonies were of comparable Quality (test item: 8379 to 13316 bees per colony, control: 8255 to 15316 bees per colony). All colonies were increasing in size and Quality during spring. Overall the colonies of the TMX-treated group still had higher Quality compared to the control treatment. Therefore, TMX-related differences in colony Quality in the TMX-treatment were comparable to those for the control colonies during the experimental phase of the study from May 2010 up to March 2011. After overwintering in spring 2011, all test item treated colonies were from approximately the same Quality except one colony (T3: 5509 bees), which was of a lower Quality than the others.	
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7-11. Effects on colony Quality – brood development (eggs, larvae, capped cells) & food stores (honey & pollen)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. The mean percentage comb coverage of brood (eggs, larvae and pupae) and food (nectar and pollen) in the colonies showed approximately the same development in the control and the treatment group in 2010 (Tables 16-19; Figures 4-5, 8-19). During spring 2010 the colonies were increasing their brood nest size (amount of brood, number of brood combs) because of a good food supply from spring flowering plants. From the assessment start in May 2010 to end of July 2010 most of the colonies showed a clear increase in the amount of nectar on combs in the colonies (test item: T1, T2, T4, T5 and T6, control: C1 to C6), except colony T3 that had a lower amount of food (nectar) compared to the other colonies (Figure 5). On 25 August 2010 honey was harvested in colonies T1, T2, T4, T5, T6, C1, C2, C3, C4 and C6, resulting in a significant decrease in the amount of nectar in the colonies was recorded. Bee colony development, measured by a comprehensive and thorough observation that recorded hive Quality, brood and food development, overwintering success and colony health was comparable between the treated and untreated control groups.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints.	**0**

(survival and/or reproduction, and fitness)		
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 12. Effects on colony Quality – overwintering		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. However, no test item related difference in survival of the colonies in the TMX treatment compared to the control colonies was observed during the experimental phase of the study from 5 May 2010 until 25 March 2011. All colonies were well supplied with pollen and nectar after overwintering. After overwintering at the first assessment on 25 March 2011, all colonies, except one control colony (C1) had started their breeding activity. The test item colonies had higher amount of brood than the control colonies.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA)	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects	**0**
Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 13. Effects on colony health – pests, disease and parasites		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were reported. There were occasional infestations of *Nosema* spores occurring in varying degrees in all colonies. Only colony C5 had infestation in the before overwintering samples. The *Varroa* mite infestation was low in all colonies *Malpighamoeba mellificae* was found in three control colonies, and no *Paenibacillus larvae* were found (Appendix 1). CBPV, KBV, and SBV were not detected in any of the samples taken in 2010 and 2011. DWV was detected in one control sample (C4) in two samples of the test item group (T1 and T5) at the start of overwintering (Appendix 2). However, since these colonies were in a good health condition after overwintering, it can be concluded, that virus infection did not have a significant effect on bee health during the study.	**0**
Concentration- or dose-response	There was only one TMX field and 1 control field with 6 colonies at each site (pseudo-replication); therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no apparent adverse effect was observed, there was no relevance to the effects on apical endpoints.	**0**

Mechanism and or mode of action of effect explained	Since no apparent adverse effect was observed, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

No honeybees were observed collecting or taking up guttation liquid from maize or weed plants in the control field during the whole time of guttation observation. During 25 assessments, out of 149 in the test item treated plot, 13 bees were observed on maize plants and 39 bees were on the soil surface. Additionally, 40 bees were recorded on plants in the off-crop area and 66 bees on the soil surface. In one of the 4 m² areas of the test item treated field one bee was observed taking up guttation liquid from maize plants.

Expert Judgement		
QA	Yes	May 31, 2016
SEJ	Yes	May 31, 2016

(Syngenta 2013a)
Report: Syngenta. 2013. Thiamethoxam - Monitoring of Potential Effects of the Drilling of Thiamethoxam FS Treated Maize Seeds on Honeybees, Guttation Monitoring of Maize Seedlings under Agronomic Use Conditions and Assessment of the Relevance of Guttation for Honeybees in Alsace (France). Bracknell, Berkshire, United Kingdom: Syngenta Ltd. (Unpublished Report). Report CGA293343_11583 - A9807F. 1122 p

The objective of this study was to determine the effects of residues of thiamethoxam (TMX) in dust generated during maize seeding and residues in guttation liquid on honeybee colonies under field conditions. Conclusions: Over the entire observation period, exposure of honeybees (*Apis mellifera* L.) to dust generated during drilling and to fluids from maize showing guttation from seeds treated with TMX, no effect on honeybee mortality, activity, brood development and behaviour was attributed to the TMX treatment.

Responses 1-9: Quality of methods		**Score**
Experimental design and hypotheses	The study was conducted in Northern and Southern Alsace, France. TMX pre-treated seeds were sown on 19 fields (TMX fields, T1 to T19) in the spring of 2010 (all fields in April except C3 which was sown in May 2010). Additionally, three control fields (C1 to C3) were drilled with untreated maize seeds. Eight TMX fields and one control field were in Northern Alsace, 11 TMX and two control fields in Southern Alsace. The sizes of the fields ranged from 1.1 to 10.0 ha. Eight TMX and one untreated control field were near Pfaffenhoffen in Northern Alsace (T9, T13 to T19 and C2) and 11 TMX and 2 control fields close to Ueberstrass in Southern Alsace (T1 to T8, T10 to T12, C1 and C3) (Figure 90). Maize varieties (p 45-46) differed among fields and seeding rates varied from 92,000 to 105,000 seeds/ha to accommodate the drilling machines. Control fields received maize seeds treated with either thiram or a mixture of thiram, metalaxyl M, and fludioxonil; whereas, the TMX (Cruiser 350 FS) fields received either a mixture of TMX, metalaxyl M and fludioxonil; TMX, thiram, fludioxonil, and metalaxyl M; or TMX, tritconazole, thiram, fludioxonil and metalaxyl (Section 3.1; Tables 24-42 for TMX treatments; Tables 43-45 for control treatments). Four commercial honeybee colonies were placed close to each test field up to 44 d before seed drilling and maintained at the test fields between 18 and 53 d thereafter. The honeybee colonies contained approximately 3500 to 14,500 honeybees per honeybee hive. The mean colony Quality was similar between the TMX (T) and the control (C) (approximately 7200 honeybees per hive in T and approximately 8600 honeybees per honeybee colony in C). Some colonies were destroyed in a hailstorm 18 and 32 days after exposure (T13; T9 and 14, respectively). Honeybee sources were not identified Hives were maintained using good apicultural practices (p. 48). Food was provided when natural source depleted by feeding with artificial food to ensure its viability (Tables 178 to 199). The honeybee colonies were monitored for potential effects of TMX-containing dust emanating from the seed treatment coating. The second focus of the study was to examine guttation of maize seedlings at the test fields as well as potential effects of guttation droplets from treated plants on honeybees. The experimental phase of the study started with the first brood assessment before installation of the bee hives at the field sites (T1 to T19 and C1 to C2: April 2010, C3: May 2010) and ended 3.5	**3**

	months afterwards with the last brood assessment (T1 to T8, T10 to T19 and C1 to C3: July 2010, T9: June 2010). Assessments (n = 5) and beekeeper checks (every 5 to 10 d) entailed monitoring for occurrences of pests, pathogens, or disease (e.g. presence of dead honeybees, dark "bald" bees, "crawlers" or flightless bees, unusual brood patterns or brood age structure) and clear symptoms of disease (e.g. chalk brood, sacbrood, *Nosema* sp., American or European foulbrood) or pests (e.g. *Varroa* sp., *Aethina tumida, Tropilaelaps* spp.). Assessment endpoints included: mortality, flight activity of the honeybees, potential interactions of honeybees with guttation droplets and the condition of the colonies assessed during the period of drilling and up to 53 days after the emergence of the maize seedlings. Assessments of colony brood development were conducted once before the installation of the hives at the fields and three (T9), four (C1, C2, T3 to T19) or five times (T1, T2), respectively, during the hives exposure period in the treatment fields. Dead honeybees were collected from dead bee traps attached to the front of each hive for the determination of mortality. The dead honeybees were counted and, in some circumstances, retained for analysis of potential residues. Samples of honeybees were also collected from within the hives to determine the presence of bee diseases (n = 60 bees per hive; p. 54). The influence of the test item treatment was evaluated by comparing the data of the test item treated fields to those of the control; however, no statistical procedures were applied to the data (***major weakness***). Methods for collecting data and samples were either described in detail or cited in this report (see subsection 3.5). Meteorological data were recorded and reported (Tables 201-224). Assessment methods were described in detail (Subsection 3.5). Historical pesticide use of all field sites was provided (Tables 225-246). Water sources, flowering crops and weeds were surveyed (Table 200). Storage & shipping conditions and handling of samples were provided; soils were characterized (Table 271); all analytical chemistry and results were provided under separate report and were GLP compliant.	
Use of GLP and QA/QC.	This non-GLP study was conducted in the spirit of GLP and followed the Commission Directive 96/68/EC (1996) amending Council Directive 91/414/EEC and OEPP/EPPO Guideline No. 170 (3) (2001)[4]; EU 91/414/EEC (1991); study plan, deviations, method descriptions, raw data timing of events were provided.	**3**
Exposure concentrations	Application rates were similar among TMX treated fields. Residues were measured in honeybees, nectar, pollen and guttation fluid, soils and plants and results summarized in the text provided.	**4**
Transparency of data.	Raw and summary data were comprehensively provided.	**4**
Number of samples and replication.	There were two treatments: TMX and control with 19 and 3 independent fields divided between the northern and southern areas of Alsace region in France. Each field had 4 honeybee colonies. Multiple sampling events and measurements occurred overtime time.	**4**
Overall evaluation of methods		**3.60**
Score for expert judgment on quality of the study- no statistical procedures were applied to the data **(*major weakness*)**	**0.5**	**1.80**

Response 1. Effects on mortality of honeybees – dead bee traps and linen sheets.		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. Mortality data are summarized in Tables 47-67. On the day after drilling an increase in honeybee mortality, compared to mean mortality before drilling, was observed in one test item treated field (T6) which was attributed to the effects of an unidentified pesticide applied on the day of drilling to an adjacent field. Throughout the entire assessment period 636, out of a total of 5332, observations of test item treatment hives showed an increase in honeybee mortality for individual hives (Figures 23 to 44). Of these 636, 120 occurred prior to seed drilling. For the control hives 77, out of 820, observations demonstrated increased honeybee mortality. Eighteen of these occurred prior to seed drilling. The higher mortality values were observed before and after drilling of maize seed at the field and in general correlated with inclement weather, such as cold weather and precipitation events, and with the timing of hive observations, such as brood assessments or beekeeper checks. When honeybee mortality was recorded using a dead bee trap installed at the hive, the mortality rate generally increased during inclement weather conditions (see Figures 1 to 22). This can be attributed to the fact that enervated honeybees, which usually fly out before their expiration, die inside of the hive and are subsequently removed "en masse" from the hive by worker honeybees the next time weather conditions are suitable. Similarly, brood assessments and beekeeper checks inevitably cause honeybee mortality due to individual honeybees becoming trapped or injured during the procedure and hence an increase in honeybee mortality can be expected following such operations. When considering the mortality rates of the entire assessment period, no test item related difference in mortality in the test item fields compared to the control fields was observed.	**0**
Concentration- or dose-response	Although there were 19 TMX-treated fields and 3 TMX-free fields, the same concentration was applied to these fields. Therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 2-3. Effects on flight activity and behavior of honeybees – hive entrance & in field assessment areas		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. No abnormal behaviour of the honeybees in front of the hives was observed during the entire observation period except for some clustering honeybees at the entrance of the hive and aggressiveness on two days, which was most likely due to weather conditions (Tables 90-111). No honeybees were observed in any of the control fields. Three out of the 18 honeybees, observed in the TMX fields, showed symptoms of intoxication, such as cramping or	**0**

	uncoordinated movements. All other honeybees behaved normally. In the off-crop areas adjacent to the test item fields, five honeybees were observed, two of them were taking up guttation droplets (T12). All five honeybees showed a normal behavior. The flight activity was similar between the colonies of the TMX treatment and control, although it varied strongly between single hives and different dates.	
Concentration- or dose-response	Although there were 19 TMX-treated fields and 3 TMX-free fields, the same concentration was applied to these fields. Therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 4-6. Colony Quality – brood development (egg, larvae, capped brood cells)		**Score**
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. Generally, the mean surface areas of brood (eggs, larvae, and pupae) in the test item and control colonies increased in size during the study, except following several natural and external factors such as swarming, queen loss during transport and a male brood producing queen. Because of swarming, the mean development plateaued or slightly decreased in the middle of May or June. All colonies that swarmed demonstrated normal development according to the following brood assessments, i.e. new egg-laying queens were reared. Colony development, measured by a comprehensive and thorough observation of colony Quality, brood and food development and colony health was similar between the test item treatment and the control. No effect of residues of TMX and clothianidin in dust generated during maize seeding on honeybee colonies was observed. Figures 45 to 66 show the areas of brood (egg, larval and capped cells) in the bee hives of the test item and control fields (T1 to T19 and C1 to C3) during the entire study period.	**0**
Concentration- or dose-response	Although there were 19 TMX-treated fields and 3 TMX-free fields, the same concentration was applied to these fields. Therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 7-8. Effects on food stores – hive nectar and pollen		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. Figures 45 to 66 show the areas of food (nectar and pollen) storage in the bee hives of the test item and control fields (T1 to T19 and C1 to C3) during the entire study period. Test field values for individual hives as well as average values of all four hives on the test field are shown. No TMX-related effects on food storage were apparent. There were no noticeable differences between the colonies of the TMX treatments and those from the control fields when comparing food storage (nectar and pollen).	**0**
Concentration- or dose-response	Although there were 19 TMX-treated fields and 3 TMX-free fields, the same concentration was applied to these fields. Therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Response 9. Effects on colony Quality – # honeybees per hive		Score
Statistical significance of responses	No statistical procedures were applied to the data and no P or r^2 values were provided. In general, the Quality of the colonies (number of honeybees in the hive) increased in both treatments over the observation period (mid-April to end of July, 2010) and the test item colonies were all in the range of the mean values of the three control groups.	**0**
Concentration- or dose-response	Although there were 19 TMX-treated fields and 3 TMX-free fields, the same concentration was applied to these fields. Therefore, a concentration-exposure response was not applicable (NA).	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Since no adverse effect was apparent, there was no relevance to the effects on apical endpoints.	**0**
Mechanism and or mode of action of effect explained	Since no adverse effect was apparent, no mechanism or mode of action was proposed.	**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

The occurrence of guttation in both the crop and off-crop areas was influenced by the weather conditions, i.e. absence of wind, high humidity and low temperatures advanced the appearance of guttation droplets. Generally, the extent of guttation was similar in the test item and control fields. Guttation events were greater in the morning before 8:00 than later in the day (on 86.5 % of the assessments in the control fields and on 84.3 % in the treatment fields). Guttation after midday assessments occurred on 26 % of the assessments in the control fields and on 21.7 % in the treatment fields. In the evening, guttation occurrence slightly increased again, it was

observed in 37.9 % of all assessments in the control fields and in 35.4 % of the assessments in the treatment fields.

Residues of TMX and CTD in honeybee samples were detected in the range below the limit of quantification (0.0001 mg/kg) to 0.0280 mg/kg and (0.0001 mg/kg) to 0.0547 mg/kg, respectively. Residues of TMX were detected in the range below the limit of quantification (0.0001 mg/kg) to 0.00071 mg/kg in several untreated control honeybee samples (dead honeybees in front of the bee hives). In case CTD residues in untreated control bee samples were detected in the range below the limit of quantification (0.0001 mg/kg) to 0.0014 mg/kg[2]. Low levels of residues were specific to single bee hives; no residues were found in the control samples. On two sampling days (13 and 17 May 2010), small amounts of TMX were found in honeybee samples of bee hive 4C3. These findings were attributed to honeybees foraging on other plant species potentially subjected to TMX applications independent of this study.

Expert Judgement		
QA	Yes	June 4, 2016
SEJ	Yes	June 5, 2016

(Stanley et al. 2015)

Paper: Stanley J, Sah K, Jain SK, Bhatt JC, Sushil SN. 2015. Evaluation of pesticide toxicity at their field recommended doses to honeybees, *Apis cerana* and *A. mellifera* through laboratory, semi-field and field studies. *Chemosphere* 119:668-674.

The objective of this three-tiered study was to examine the toxicity of a foliar application of thiamethoxam (TMX) (among other insecticides) to *Apis cerana and Apis mellifera* (honeybee) using acute toxicity tests, semi-field (caged-pot) trials, and field studies. The resulting toxicity of TMX to honeybees observed from acute and semi-field studies precluded performing the field studies with TMX.

Response 1: Quality of methods		**Score**
Experimental design and hypotheses	The studies occurred at an agricultural station (VPKAS) in Hawalbagh, India in the state of Uttarakhand. The WoE herein is focused on the semi-field and field studies. The recommended label rate for TMX use was 0.25 mL/L for Actara 25 WG, so the concentration 50 ppm (mL/L or mg/kg) was used (Table 1). Tier 1 - The results of the acute toxicity (Table 2) indicated that TMX was toxic to both species of honeybees using filter paper contact tests and topical assays (methods described in detail). The 48-h percent mortalities for *A. cerano* exposed to TMX via filter paper disc and topical application were 26.67 and 100%, respectively (Table 2). The acute mortalities (48-h) for *A. mellifera* were 73.33 and 100%, respectively. Tier 2 – The methods were well described and involved mustard plants in pots (var. VLT-3) sprayed with TMX using a hand sprayer (no calibration) to drench the plants which were allowed to dry for an hour before being placed into a mustard field where both species of honeybee would have access. The number of exposure concentration was not mentioned so the assumption was that only one application was used (label rate recommended for use on mustard). There were four pots per treatment replicate. 16 pots were divided into 4 groups of four and 3 groups were placed inside three 1 m^2 quadrates (4 pots per quadrate) and covered with mosquito netting while the fourth group of four remained uncovered with open access to bees in the field. The honeybees were collected after visiting at least 2 flowers from sprayed pots and placed into test tubes. Five of these bees from each species were released into each quadrate and allowed to forage for 1 hour; there was a total of 20 bees of each species. After 1 hour, the bees were collected back from each quadrate and kept in separate jars (provided with cotton-tissue paper cubes dipped in sugar solution) and bee mortality was recorded at 1, 24 and 48h. There was no confirmation of dosages (***major weakness***) and no chemical analysis of residues on plants or in bees (***major weakness***). There was no mention of a control treatment (***major weakness***). Results of the semi-field study with TMX indicated that TMX was toxic to both species of bees. For *A. cerano* and *A. mellifera,* 85 and 95% mortality occurred within an hour of exposure and after 24 h, all were dead.	**1**
Use of GLP and QA/QC.	Not a GLP study and no QA/QC mentioned	**0**
Exposure concentrations	Only label rates provided for TMX as Actara 25 WG; no analytical chemistry to confirm exposure	**0**

Transparency of data.	Only % mortality data were presented without mention of experimental controls		**0**
Number of samples and replication.	It was unclear if plants were sprayed independently; suspect that pseudoreplication and only one field plot was used.		**0**
Overall evaluation of methods			**0.20**
Score for expert judgment on quality of the study- no confirmation of dosages; no residues were measured; no control treatment (all **major weaknesses**)		**0.125**	**0.03**

Response 1. Effect of TMX on mortality of two species of honeybees in semi-field study		**Score**
Statistical significance of responses	Mortalities were compared to those for other insecticides not to experimental controls.	**0**
Concentration- or dose-response	Not applicable (NA) because only label rate used.	**NA**
Relevance of effect to apical endpoints (survival and/or reproduction, and fitness)	Given this experimental set up the data cannot be used in a weight of evidence analyses.	**0**
Mechanism and or mode of action of effect explained		**0**
Overall evaluation of relevance (computed)		**0.00**
Overall evaluation of relevance (SEJ).		

Narrative

No useful effects data provided for WoE analyses. This was not a dust study; foliar application only. This also was not a seed study; foliar application only.

Expert Judgement		
QA	Yes	June 1, 2016
SEJ	Yes	June 2, 2016