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WASHINGTON D.C., 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: **Thiamethoxam**: Addendum to the Non-Pollinator Draft Risk Assessment (DRA) and Response to Public Comments Received on the Bee and Non-Pollinator DRAs

FROM: Kristina Garber, Senior Science Advisor
Chris Koper, Chemist
Environmental Risk Branch 1

KRISTINA GARBER Digitally signed by KRISTINA GARBER Date: 2020.01.07 08:27:45 -05'00'

2020.01.06 08:47:41 -05'00'

Ryan Mroz, Biologist/Risk Assessment Process Leader
Environmental Risk Branch 5
Environmental Fate and Effects Division (7507P)

RYAN MROZ 2020.01.06 08:32:47 -05'00'

THRU: Sujatha Sankula, Branch Chief
Gregory Orrick, Risk Assessment Process Leader
Environmental Risk Branch 1
Environmental Fate and Effects Division (7507P)

Sankula, Sujatha Digitally signed by Sankula, Sujatha Date: 2020.01.06 11:02:21 -05'00'

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TO: Matthew Khan, Chemical Review Manager
Marianne Mannix, Team Leader
Dana Friedman, Branch Chief
Risk Management and Implementation Branch 1
Pesticide Re-evaluation Division (7508P)

The Registration Review process for the neonicotinoid insecticide thiamethoxam has been phased, with release of honey bee and non-pollinator draft ecological risk assessments (DRA) at different times, with individual public comment periods. Additionally, the registration review of thiamethoxam has been closely aligned, in timing and risk assessment methodology, with the registration review of three other nitroguanidine-substituted neonicotinoids (*i.e.*, imidacloprid, clothianidin, and dinotefuran). **Table 1** provides a summary table of the risk assessment documents and docket numbers associated with each of the four neonicotinoids. The term "preliminary risk assessment" (PRA) was in use for earlier assessments but has been recently replaced with the term "draft risk assessment" (DRA).

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Table 1. Risk assessment documents for nitroguanidine-substituted neonicotinoids.

	Pollinator / Bee Risk Assessment	**Non-pollinator Risk Assessment(s)**
Imidacloprid	Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. (DP 429937, 1/4/2016) Docket ID: EPA-HQ-OPP-2008-0844-0140 Final Bee Risk Assessment to Support the Registration Review of Imidacloprid. (DP 443668, 1/2020) Docket ID: EPA-HQ-OPP-2008-0844-xxxx	Preliminary Aquatic Risk Assessment to Support the Registration Review of Imidacloprid. (DP 435477, 12/22/2016) Docket ID: EPA-HQ-OPP-2008-0844-1086 Preliminary Terrestrial Risk Assessment to Support the Registration Review of Imidacloprid (DP 442830, 11/28/2017) Docket ID: EPA-HQ-OPP-2008-0844-1256
Clothianidin	Preliminary Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. (DP 437097, 1/5/2017) Docket ID: EPA-HQ-OPP-2011-0865-0173 Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. (DP 455645, 1/2020) Docket ID: EPA-HQ-OPP-2011-0865-xxxx	Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support the Registration Review of Clothianidin. (DP 439290, 11/27/2017) Docket ID: EPA-HQ-OPP-2011-0865-0242
Thiamethoxam	Preliminary Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. (DP 437097, 1/5/2017) Docket ID: EPA-HQ-OPP-2011-0581-0034 Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. (DP 455645, 1/2020) Docket ID: EPA-HQ-OPP-2011-0581-xxxx	Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support the Registration Review of Thiamethoxam. (DP 439307, 11/29/2017) Docket ID: EPA-HQ-OPP-2011-0581-0093
Dinotefuran	Draft Assessment of the Potential Effects of Dinotefuran on Bees (DP 437374, 1/3/2017) Docket ID: EPA-HQ-OPP-2011-0920-0014 Final Bee Risk Assessment to Support the Registration Review of Dinotefuran. (DP 451015, 1/2020) Docket ID: EPA-HQ-OPP-2011-0920-xxxx	Preliminary Ecological Risk Assessment (excluding terrestrial invertebrates) for the Registration Review of Dinotefuran. (DP 441527, 11/28/2017) Docket ID: EPA-HQ-OPP-2011-0920-0616

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The purpose of this document is to respond to thiamethoxam-specific public comments received on the draft honey bee and draft non-honey bee risk assessments for Registration Review. Also, this document serves as an addendum to the preliminary non-pollinator DRA, where additional modeling or risk quotient corrections were needed, or where additional characterization or impacts to risk conclusions are discussed. For the honey bee DRA, thiamethoxam-specific comments were submitted by Syngenta (the technical registrant of thiamethoxam). Updates and responses noted in this document to thiamethoxam-specific comments on the draft bee risk assessment, have been incorporated into the *"Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam"*.

For responses to public comments that were common across all four noenicitinoid active ingredients for the preliminary pollinator and non-pollinator DRAs, a common response to comments (RTC) document was written. See the document, *"EFED Response to Public Comments Common to the Preliminary Pollinator and Preliminary Non-Pollinator Registration Review Risk Assessments Across the Four Neonicotinoid Pesticides (Imidacloprid, Thiamethoxam, Clothianidin, and Dinotefuran)"*. For chemical-specific responses to comments for imidacloprid, clothianidin, or dinotefuran, please see their chemical-specific RTC documents in their individual registration review dockets.

This document is divided into several sections. **Section 1** responds to thiamethoxam-specific public comments on the preliminary bee DRA. **Section 2** responds to thiamethoxam-specific public comments on the preliminary non-pollinator DRA. **Section 3** is an addendum that includes updated aquatic environmental exposure concentrations (EEC) and risk quotients (RQ) for seed treatment uses of thiamethoxam. Additional updates to the aquatic invertebrate RQs are provided in a separate memo (***Comparative analysis of Aquatic Invertebrate Risk Quotients generated for neonicotinoids using Raby et al. (2018) toxicity data***; **DP 455690**) that summarizes the review and integration of new acute and chronic invertebrate data published by Raby *et al.* in 2018[1,2].

EFED generally uses an outline format to address comments (comment followed by EFED response). The full text of the public comment submissions can be found in the thiamethoxam docket at www.regulations.gov (EPA-HQ-OPP-2011-0581).

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[1] Raby, M; Nowierski, M.; Perlov, D; Zhao, X.; Hao, C; Poirier, D.G. and P.K. Sibley. 2018a. Acute Toxicity of 6 Neonicotinoid Insecticides to Freshwater Invertebrates. Environmental Toxicology and Chemistry, 37 (5): 1430–1445. MRID 50776401.

[2] Raby, M; Zhao, X.; Hao, C.; Poirier, D.G. and P.K. Sibley. 2018b. Chronic toxicity of 6 neonicotinoid insecticides to Chironomus dilutus and Neocloeon triangulifer. Environmental Toxicology and Chemistry, 37 (10): 2727-2739. MRID 50776201.

Section 1. EFED Response to Thiamethoxam-specific Public Comments on Preliminary Bee Risk Assessment

This section responds to thiamethoxam-specific public comments that were received on the *"Preliminary Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam"* (DP 437097; 1/5/2017; Docket ID: EPA-HQ-OPP-2011-0581-0075).

Comments from Syngenta Crop Protection, LLC.

Comments submitted specifically for thiamethoxam from Syngenta were organized into the following categories.

- The use of clothianidin equivalents (regarding differential toxicity between clothianidin and thiamethoxam)
- Colony feeding study (CFS)
- Bee bread use in the risk assessment
- Assessment of pollinator risk from off-field drift
- Incident reports and other lines of evidence
- Specific comments and proposed error corrections

Many of the concepts brought up in these sections of Syngenta's comment document have been addressed in the updated risk assessment including: a justification for using clothianidin equivalents, incorporation of a new colony feeding study in addition to the original submission, incorporating additional tier I toxicity, residue in pollen and nectar studies to address previous uncertainties, and a newly developed method to assess pollen exposure to honey bee colonies (which supersedes the "bee bread" method used in the preliminary assessment). Additionally, comments about spray drift and incidents are addressed in the general response to comment document for all 4 neonicotinoids. Below are the thiamethoxam-specific comments addressed by EFED, many of which are more fully addressed in the updated RA and general RTC document.

Syngenta Comment - EPA converted all thiamethoxam bee toxicity endpoints and residue concentrations in pollen and nectar to clothianidin equivalents given that clothianidin is a major degradate of thiamethoxam and based on the assumption that the toxicity of clothianidin and thiamethoxam are similar for bees. However, the standard toxicity studies with both terrestrial (*i.e.*, bees) and aquatic invertebrates indicate a clear difference in chronic toxicity between clothianidin and thiamethoxam. In addition, recent laboratory chronic toxicity data show significant differences in adult bee sensitivity to thiamethoxam versus clothianidin. Considering the chronic toxicity of clothianidin to bees is not similar to thiamethoxam, the use of clothianidin equivalents is not appropriate. Syngenta recommends using the Toxic Unit (TU) approach to assess potential risk to individual bees consuming pollen and nectar with residues of both clothianidin and thiamethoxam and that the total TUs can be summed based on in-hive worker bees that consume the most pollen (10% of their diet) and nectar foragers that consume the most nectar (100% of their diet).

> **EFED Response** - As indicated in the revised assessment, (**Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam; DP 455645**) EFED's analysis indicates thiamethoxam and clothianidin are of similar toxicity to bees on an acute basis and

have comparable effects at similar concentrations. Therefore, the toxic unit approach suggested by Syngenta is not warranted.

Summarized comments regarding the colony feeding study: Syngenta believes the thiamethoxam colony feeding study was not evaluated similarly to the colony feeding studies for the other neonicotinoids and provided a justification for the noted uncertainties in the evaluation of that study. Syngenta also noted another CFS was completed and submitted to the Agency.

EFED Response: EFED's review of the first colony feeding study (CFS) noted statistically significant effects in several test levels and due to a lack of successful overwintering left sufficient uncertainty to determine if these effects were transient or colony level effects (MRID 49757201). As noted above, a second CFS was conducted by Syngenta, submitted to, and evaluated by EFED for the final bee assessment (MRID 50432101). This study was classified as acceptable, considered scientifically sound and suitable for quantitative use in the final risk assessment. Both studies provide valuable information on effect levels for understanding colony level risks to honeybees from thiamethoxam and were used in risk analysis in the updated final pollinator assessment. The second CFS showed consistent sustained effects to honeybee colonies at similar levels to those found in the first study.

Syngenta Comment - Thiamethoxam is a systemic compound and moves within the xylem of the plant; however, Syngenta disagrees with the Agency's statement that thiamethoxam is also phloem-mobile. Detection of thiamethoxam and clothianidin in pollen and nectar when applied via soil and seed treatment methods demonstrate that these compounds are xylem mobile. Detections in pollen and nectar from foliar applications are likely the result of flower bud material being sprayed directly prior to bloom rather than movement of thiamethoxam from leaf to flower tissue.

EFED Response: EFED agrees that the evidence supporting thiamethoxam mobility in xylem is evidenced by the soil and seed treatment residue studies. However, these studies do not provide sufficient design elements to evaluate potential mobility in phloem. EFED assumes that residues in nectar and pollen are potentially derived from both xylem and phloem contributions. This is based on several biological considerations: Nectaries are anatomically different across monocots and dicots such that some have direct connectivity to vascular tissues and others do not have direct vascular system connections; the anther and pollen sac are both directly fed by xylem and phloem vascular tissues. Therefore, the presence of thiamethoxam and clothianidin in pollen and nectar can be the result of either one or both xylem and phloem transport. Furthermore, there is evidence that insects feeding on phloem can secrete contaminated honeydew from plants treated with neonicotinoids (Calvo-Agudo et al, 2019[2]). This suggests thiamethoxam movement in phloem. EFED acknowledges there is uncertainty in the relative magnitude of phloem vs xylem concentrations and how that may ultimately impact pollen and nectar concentrations. However, because the residue studies capture thiamethoxam and clothianidin transport on a whole plant basis (vascular and non-vascular), EFED is less concerned about individual pathways leading to the empirically measured concentrations. Ultimately, the availability in phloem to potential feeders and potential contribution to concentrations in nectar are appropriate for consideration in risk assessment.

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[2] Calvo-Agudo, M., J. González-Cabrera, Y. Pico, P. Calatayud-Vernich, A. Urbaneja, M. Dicke, and A. Tena. 2019. Neonicotinoids in excretion product of phloem-feeding insects kill beneficial insects. Available at: www.pnas.org/cgi/doi/10.1073/pnas.1904298116

Syngenta Comment - Normalizing the citrus pollen and nectar residue data to 0.172 lb ai/acre (maximum soil application rate) assumes that the residues detected in pollen and nectar is linearly correlated with application rate. For soil applications, other variables including soil type and characteristics, rainfall, timing of application, and tree density also have an influence on measured residues in both pollen and nectar. Therefore, without a verification of a linear relationship between application rates and the residues detected, the residue data should not be normalized to a single rate and only data for the maximum application rate (0.172 lb ai/acre) or lower should be used in the assessment.

> **EFED Response**: EFED acknowledges there are many types of factors like those noted above that could influence (either increase or decrease) the potential residues in pollen/nectar after soil applications. Because a model to account for these factors was not available in order to make use of the most data points for residue analysis, the data were normalized. Normalizing the data is a noted uncertainty; however, it was done in an attempt to most completely utilize the available data. This issue was further considered in Attachment 2 to the Final Pollinator Risk Assessment and, for citrus studies conducted at the same location with different application rates, the linear scaling assumption was determined to be appropriate.

Syngenta Comment - The canola study cited (MRID 49819502) was designed to determine if soil applications to potato would carry over to pollen and nectar residues in thiamethoxam seed treated canola. Canola grown from untreated seed in plots that were treated the previous year with a soil application of thiamethoxam had similar pollen residues to canola grown from treated seed. The untreated controls also had similar pollen residues levels which suggests that the pollen residue levels may not be the result of the thiamethoxam seed treatments. In addition, there was only one sampling interval for the study and, therefore, a chronic EEC based on multiple sampling intervals cannot be used. Given the uncertainty in this study, pollen and nectar residue data from a separate canola study (MRID 49775702) should be used in the refined assessment.

> **EFED Response**: The seed treatment risk assessment analysis has been updated to include MRID 49775702.

Syngenta Comment - We appreciate that the Agency is likely using clothianidin equivalents to compare application rates between clothianidin and thiamethoxam. However, presenting the single application rate as clothianidin equivalents gives the impression that efficacy is directly related to the presence of clothianidin rather than the parent thiamethoxam.

> **EFED Response**: The use of clothianidin equivalents was not intended to attribute efficacy of that chemical to thiamethoxam, but strictly for a single currency throughout the document to avoid switching from different active ingredient and units. This point is clarified in the final bee assessment.

Syngenta Comment - Syngenta also recommends using dietary-based endpoints (LC50 and NOAEC) from the larval toxicity studies as the dose is based on a cumulative exposure and a daily dose cannot be estimated from these studies since diet is not completely consumed until the end of the larval phase (and if food is still present it is noted in the study report). Other reasons we recommend using concentrations for the larval endpoints include: 1) consumption by the larvae is exponential during the growth phase and only food consumption for 5-day old larvae is considered in the risk assessment, 2)

the consumption rates for laboratory larvae should be similar to larvae in the field (hives), and 3) endpoints can be compared directly with pollen and nectar residue concentrations.

> **EFED Response**: The methodology used in the assessment relies on dose-based endpoints, which is consistent with the 2014 pollinator risk assessment framework and BeeREX model.

Syngenta Comment - Overall, the number of incidents appears to be quite low given the extent of use of thiamethoxam in the U.S. over the 17 years it's been registered in the U.S. which is a testament to the safe use of thiamethoxam products by growers and the continued stewardship provided by Syngenta.

> **EFED Response** – EFED appreciates Syngenta's comment regarding stewardship (also below). Incidents are incorporated into the risk assessment as a line of evidence when considering the potential for risk from the registered use patterns. The absence of reported incidents should not be construed as the absence of incidents. Incident reports for non-target organisms typically provide information only on mortality events, while sublethal effects in organisms such as abnormal behavior, reduced growth and/or impaired reproduction are rarely reported. EPA's changes in the registrant reporting requirements for incidents in 1998 may account for a reduced number of reported incidents as only detailed information on "major" fish, wildlife, and plant incidents are required. Minor incidents are generally reported aggregately. In addition, there have been changes in state monitoring efforts due to a lack of resources. However, for some use patterns, the incident data that are available suggest that exposure pathways for thiamethoxam to reach non-target organisms are complete and that exposure levels are sufficient to result in field-observable effects.

Syngenta Comment - Seven incidents have been reported in association with corn planting in Indiana, Minnesota and Illinois. As mentioned in the report, exposure of bees to clothianidin and thiamethoxam via drift of abraded seed coat dust is considered a route of concern, but "the Agency is working with different stake holders to identify best management practices and to promote technology-based solutions that reduce this potential route of exposure." Minimizing dust drift resulting from planting treated seed is among the highest priorities for Syngenta. Examples of our extensive efforts in this regard include our ongoing efforts to develop and optimize new seed treatment formulations and tank-mix recipes to minimize dust abrasion through the use of new and improved dust reducing agents and polymers. In addition, at our new, state-of-the-art Syngenta Seedcare Institute, we provide extensive applicator training to our Seedcare customers, including seed companies and treaters, on how to properly handle, and apply, our products during seed treatment. Further, we offer technical assistance to these same customers at their treatment sites when questions and/or issues arise to ensure our seed treatment products are properly applied. Through our sales and seed advisor staff, we educate growers on the best way to handle and plant treated seed to minimize dust abrasion and dust-off at planting as well as disposing leftover treated seed properly. Syngenta also conducts extensive research in seed treatment application technology to determine the best seed processing steps (*i.e.*, cleaning seed before treatment to remove seed generated dust) all the way to evaluating and optimizing droplet/particle sizes during seed treatment application to ensure our products stay on the seed while handling and planting to minimize dust-off.

> **EFED Response**: Thank you for the information regarding stewardship and minimizing drift. The Agency will continue to be involved with stakeholders in the drift reduction discussion through avenues such as stewardship practices.

Finally, there are also several comments submitted by Syngenta that suggest typographical errors, inconsistent information, and other error corrections. These comments have been considered by EFED and many resulted in updates (e.g. additional residue data and new toxicity studies), to the final bee assessment document. However, these updates do not significantly change risk assessment conclusions.

Section 2. EFED Response to Comments for Thiamethoxam-Specific Preliminary Non-Pollinator Risk Assessment Public Comments

This section responds to thiamethoxam-specific public comments that were received on the thiamethoxam *"Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support Registration Review"* (DP 439307; 11/29/2017; Docket ID: EPA-HQ-OPP-2011-0581-0075). This section is broken into general/broad and specific comments submitted by syngenta.

Syngenta comments on aquatic exposure monitoring data in the executive summary

Syngenta comment - This document provides additional lines of evidence to support Syngenta's position that the preliminary ecological risk assessment is overly conservative and seeks to address areas of uncertainty identified by the Agency in its use of water monitoring data. Syngenta provides a statistical analysis of all the publicly available surface water data. To account for variation across data sources in monitoring objectives and sampling designs (timing and frequency), a pooled estimation approach with time-weighting and requirement for smallest effective sample sizes was used to estimate the 90th, 95th, and 99th percentiles and confidence intervals. Results of the pooled analysis demonstrate the percentiles for the data sources of sufficient effective sample size are very low; the largest 90th and 95th percentiles are <0.025 ppb and 0.03 ppb, respectively, for thiamethoxam in the Corn Belt. The 99th percentile concentration for thiamethoxam was estimated at 0.033 ppb for the Great Lakes where there was sufficient data for the estimation. Given the availability and large amount of monitoring data sufficient to statistically derive the upper bound aquatic exposure values (at and above the 90th percentile), Syngenta encourages EPA to use these observed concentration values to reduce the uncertainties in the predicted exposure estimated by the pesticide water calculator (PWC) scenario modelling.

> **EFED Response**: Typically, available monitoring programs are not targeted to account for all thiamethoxam use areas, timing of application, and other factors which may more accurately represent spatially and temporally dependent variables influencing runoff vulnerability. In very few instances are monitoring sites sampled frequently enough to ensure that the peak concentration has been measured. As a result, EFED did not conduct quantitative comparisons of monitoring data to acute or chronic endpoints for thiamethoxam. It is also difficult to assess trends, since the measured concentrations represent snapshots in time which generally are further apart than the endpoint durations being considered. Additionally, the Screening Level and Usage Analysis (SLUA) conducted by BEAD indicates that the majority of thiamethoxam applied in the United States is via seed treatment of corn and soybean, such that the available monitoring data are probably only reflective of these labeled uses and not a reflection of other modeled labeled uses.

Syngenta comment - From an aquatic exposure perspective, Syngenta demonstrates the conservative nature of PFAM in comparison to the measured levels of thiamethoxam in paddy and receiving waters from two guideline field aquatic dissipation studies (OPPTS 835.6200). The highest seed treatment rate modelled in the preliminary ecological risk assessment is approximately 4X lower than the seed treatment rates used in the aquatic dissipation studies. Despite this, PFAM 1-day EECs in the paddy are

either on the same order of magnitude as the field-observed values (California) or greater than 13X the concentration observed at the Louisiana location. Syngenta agrees with the Agency in the use of higher-tier models, such as PFAM, to offer more refined environmental exposure estimates; however, caution should be used when interpreting the modelled exposure estimates as they consistently exceed monitoring data. Syngenta also disagrees with the Agency in focusing on exposure values from the paddy for estimating potential risk to aquatic organisms. Rice paddies are not stable aquatic habitats as they are frequently drained and rotated with terrestrial crops (*e.g.*, soybeans, cotton, corn, sorghum) which does not allow for aquatic organisms to establish stable populations. The Agency should focus on the adjacent water bodies that receive tail water from the paddies as these water bodies are likely to be more permanent and support aquatic life.

> **EFED Response**: EFED developed a methodology for evaluating risks to aquatic invertebrates using PFAM. While the model allows for the discharge of the paddy water into the standard EPA pond, this method is not employed by EFED in its ecological risk assessments, as it is not certain that this conceptual model is representative for what happens in an aquatic environment. PFAM-estimated EECs are relevant to non-target organisms in the paddy and to non-target organisms in water bodies dominated by released paddy tailwater. To the extent that released paddy tailwater is diluted by uncontaminated water, aquatic exposure in water bodies receiving tailwater will be less than estimated by PFAM.

Syngenta's comments regarding aquatic invertebrate risk conclusions using chironomus - Risk quotients (RQs) for several thiamethoxam uses exceeded acute and chronic levels of concern (LOCs) for freshwater invertebrates indicating potential risk. Acute and chronic endpoints used in the preliminary risk assessment were based on toxicity studies conducted with chironomids as this taxon was determined to be the most sensitive and therefore a conservative surrogate for all aquatic invertebrates. Although sensitive to thiamethoxam, chironomid life history and life cycle attributes allow for recovery and therefore, significant population-level effects would likely not be realized. This is also true for many other aquatic invertebrate taxa with high reproductive rates and multiple generations per year.

Additional lines of evidence including probabilities of effects using additional data and SSDs were provided.

> **EFED Response**: At this time the Agency's deterministic risk assessment under FIFRA does not account for probabilities of effects or population level impacts and additional cascading indirect effects. The noted uncertainty is that we may not have the most sensitive species accounted for, but the most sensitive species tested, and thus the potential for risk to aquatic invertebrates is evaluated using the chironomid endpoint. EFED acknowledges Syngenta's point that the most usage for thiamethoxam is from seed treatment, for which the potential for risk was considered low in the risk assessment. An additional analysis entitled: ***Comparative analysis of aquatic invertebrate risk quotients generated for neonicotinoids using Raby et al. (2018) toxicity data;*** **DP 455690** was also conducted based on an open literature study for thiamethoxam using endpoints for midges (~10x) and mayflies (~5X) that were less sensitive than the one used in the preliminary risk assessment, and came to the same conclusions for seed treatments. Taken as a whole, the data suggest that based on the exposure profile the potential for risk (e.g. risk quotients exceed the Agency's level of

concern (LOC)) exists for aquatic invertebrates from foliar and soil uses of thiamethoxam, while a lower potential exists for seed treatment uses (LOC exceedances only for seed treated rice).

Syngenta's comment regarding the potential for risks to birds and mammals - Syngenta provided an analysis of EFEDs risk assessment for birds and mammals with respect to risks from exposure to treated thiamethoxam seeds. Syngenta's position is that the overall probability of adverse effects to birds and mammals due to chronic consumption of thiamethoxam-treated seeds is very low after considering:

1. realistic estimates of the proportion of treated seeds in bird and mammal diets,
2. reduction of exposure based on seed incorporation rate of 99% with only 1% of planted seeds available for consumption by wildlife,
3. recalculation of daily dose using body weight and ingestion data from the mallard reproduction study,
4. potential lack of temporal overlap of avian breeding phenology and seed planting windows,
5. the bioenergetic realities associated with seed concern (number of seeds consumed),
6. reduced avian and mammal exposure due to seed pelleting,
7. the uncertainty associated with the avian NOEC of 300 ppm as opposed to 900 ppm,
8. reduction of exposure based on husking seeds and removal of seed parts containing greatest potential residues of thiamethoxam, and
9. the uncertainty that exposure to thiamethoxam treated seeds is chronic considering planting is typically once each year often prior to avian breeding activity and both residues and seed integrity decline quickly over time reducing probability of chronic ingestion of treated seeds.

The compounding of these factors can reduce chronic avian and mammal RQs below the LOC of 1. Therefore, considering all factors, Syngenta believes the potential acute and chronic risk concern from potential exposure to thiamethoxam treated seeds to birds and mammals is relatively low.

EFED Response: EFED's assessment was deterministic (based on RQs and conservative estimates of exposure). Many of the uncertainties noted by Syngenta are standard assumptions associated with EFED's assessments. Some of these uncertainties were characterized in the assessment (*e.g.*, estimates of the number of seeds to reach the NOAEC were included). For the standard conceptual model, EFED identified risk concerns for birds exposed to thiamethoxam from consumption of treated seeds.

Syngenta's comment on a monitoring study - Miles *et al.* (2017) report concentrations of several neonicotinoids in field collected soil and water samples. The field sampling component of the study focuses on acetamiprid, clothianidin, imidacloprid, and thiamethoxam. This response focuses on and addresses the aqueous concentrations reported for thiamethoxam. Syngenta believes the reported aqueous thiamethoxam concentrations, in both a spatial context (*i.e.*, among sites including the reference site) and temporal context (*i.e.*, across eight weekly post-planting sampling dates), are systematically and significantly elevated above previously observed environmental concentrations. This rationale is based upon several lines of evidence including: (1) the distribution of thiamethoxam surface water concentrations reported in a database

assembled from published sources for sites across North America, (2) a mass balance exercise of projected loading based on labeled seed treatment use in each watershed compared to measured water concentrations reported in the study, (3) patterns among active ingredients (*i.e.*, disproportionately higher concentrations of thiamethoxam compared to other neonicotinoids despite similar seed loading rates), and, (4) lack of plausible environmental fate mechanisms supporting patterns of soil and water concentrations (*i.e.*, that lack of detectable soil concentrations simply cannot support the reported high levels of aqueous concentrations in receiving streams in soybean or corn agroecosystems planted with thiamethoxam treated seed). A comprehensive review of the study addressing the issues stated above was formally submitted to the Agency (MRID 50425904).

A correction has recently been published (March 15, 2008) for this article addressing the errors described above https://doi.org/10.1371/journal.pone.0194634. The corrected mean and maximum concentration of thiamethoxam were 0.003 and 0.02 ppb, respectively, which fall in line with the majority of water monitoring data for thiamethoxam in surface waters.

EFED Response: EFED agrees with the lines of evidence mentioned. The corrected data coincide with the majority of the water monitoring data collected for thiamethoxam in surface waters.

Syngenta comment regarding avian endpoints - Pg. 82: Mallard reproduction study endpoints are reported as 300 and 900 mg a.i./kg-bw. These should be feed concentration levels from the study and should be reported as 300 and 900 mg a.i./kg-diet. It appears that in the calculation of $Seed_{concern}$, however, these diet concentrations have been converted to daily dose, but the actual values for body weights, food ingestion, and ultimately daily dose values are not provided within the risk assessment. Syngenta believes that the data used for these daily dose calculations should be made available to Syngenta and also requests the Agency re-check to assure appropriate weight data and ingestion rate data from the study were used in the calculation of daily dose.

EFED Response: The values used in the risk assessment were concentration-based and this is a typographical error in this section of the document. Syngenta is correct they should read as mg a.i./kg-diet. The daily dose conversion calculation equation is as follows:

$$NOAEC * ((Daily\ Food\ Intake/1000))/BW)/1000$$

The Daily food intake (g/day) is assumed to correlate with body weight using the following empirically derived equation (USEPA, 1993):

$$Daily\ food\ intake\ =\ (0.648\ *\ BW\text{^}(0.651)\ /\ (1-W)$$

Where: F = food intake in grams of fresh weight per day (g/day); BW = body mass of animal (g); W = mass fraction of water in the food (EFED uses 0.1 for granivores)

Syngenta comment regarding an aquatic endpoint - The NOEC for the Cavallaro *et al.* (2016) study stated in paragraph 1 on page 58 is 0.71 µg a.i./L, however Tables 27 and 32 report a NOAEC value for this study as 0.74 µg a.i./L. Syngenta believes the appropriate value should be 0.74 µg a.i./L.

EFED Response: The correct value is 0.74 µg a.i./L, and was the value used in the risk assessment to calculate RQs.

Syngenta comment regarding cwt calculations - There appears to be an error with the calculation of fl. oz / cwt within Table 19.

EFED Response: The correct application rates for Table 19 are below.

Table 19. Modeled Application Rates of Thiamethoxam Treated Seeds.

Crop	Product (EPA Reg.)	Application Rate (lb a.i./A)[1]	Application Rate (fl oz/cwt)	Seed Rate[2]
Sugarbeet	Cruiser (100-941)[3]	0.167	9.8	4.8
Corn		0.113	9.7	29.2
Soybean		0.083	1.3	166.7
Cotton		0.071	90	18.9

[1] Based on input from BEAD; Value used in aquatic modeling
[2] from USEPA, 2011c
[3] 47.6% thiamethoxam; density = 10.5lbs/gal

Syngenta comment regarding seed concern level - We believe the reporting of $Seed_{concern}$ for the LOAEC for soybean of 1793 is incorrect. We believe this value is too high and recommend use of the corrected daily dose for the 900 ppm treatment level that Syngenta calculated which yields a $Seed_{concern}$ for the LOAEC for soybean for a 1000 g bird as 662 seeds.

EFED Response: The calculated LOAEL estimate from a LOAEC of 900 mg a.i./kg-diet based on the previously mentioned equations is 49.57. Using this number, the actual seed concern level for large birds is 330 for soybean consumption using 0.15 mg a.i./seed (the input used in the aquatic modeling risk assessment). EFED notes Syngenta's approach is correct assuming the calculated ingestion rate from the study. It is also noted this is a characterization with all the noted uncertainties for chronic effects and seed treatments.

Section 3. Addendum to the Thiamethoxam Preliminary Non-Pollinator Risk Assessment: Revision of Seed Treatment Aquatic EECs and RQs

In 2019, EFED finalized guidance for aquatic modeling of granular and treated seed applications, to standardize EFED's surface water modeling approach. The guidance recommends using the "linearly increasing with depth" option (*i.e.*, the "triangle method") in the Pesticide Water Calculator (PWC) model, to account for seeds or granules placed at depths shallower than the incorporation depth specified on the labels. Prior to the 2019 guidance, the assumption in the PWC model (*i.e.* the "at depth" option) was that residues from treated seeds or pesticide granules placed below 2 cm were not available for runoff. Huff Hartz *et al.*[3] and Young and Fry[4] have demonstrated that when pesticide is incorporated below 2 cm, as is the case with some treated seeds, runoff of pesticide can still occur.

[3] Huff Hartz, K., Edwards, T., Lydy, M. 2017. Fate and transport of furrow-applied granular tefluthrin and seed-coated clothianidin insecticides: Comparison of field-scale observations and model estimates. Ecotoxicology (2017) 26:876–888
[4] Young, D., Fry, M. 2017. Field-scale evaluation of pesticide uptake into runoff using a mixing cell and a non-uniform uptake model. Environmental Modeling & Software 9/22/2017. https://doi.org/10.1016/j.envsoft.2017.09.007

In the non-pollinator DRAs for the neonicotinoids, risk assessors used the "at depth" option in the PWC aquatic modeling for treated seeds, which resulted in estimated exposure concentrations (EECs) equal to 0 µg/L for seeds planted at depths greater than 2 cm. **Table 1** depicts the impact on the EECs for thiamethoxam using the "triangle method" compared to the "at depth" option, as well as the range of the EECs for foliar and soil applications of thiamethoxam. The EECs with the new method range from 0.1 – 1.4 µg/L. For seed treatments that had EECs greater than 0 in the 2017 assessment, EECs increased by a factor of 2-24 times using the "triangle method", with larger increases occurring with larger depths of incorporation. While EECs for seed treatments will increase, the revised EECs are still 8-210 times lower than maximum EECs generated for foliar and soil applications.

Table 1. Comparison of Revised and Original EECs for Thiamethoxam Seed Treatment Uses

Scenario	Seeding Depth (cm)	2017 Assessment – "at depth" option					Current Approach – "triangle method"				
		Water Column EEC (ug/L)			Benthic EEC (ug/L)*		Water Column EEC (ug/L)			Benthic EEC (ug/L)*	
		1-d	21-d	60-d	Peak	21-d	1-d	21-d	60-d	Peak	21-d
MS cotton	1.27	0.51	0.42	0.26	0.10	0.09	1.18	0.97	0.61	0.23	0.22
CA cotton	1.27	0.08	0.07	0.05	0.02	0.02	0.17	0.14	0.10	0.04	0.04
MS corn	3.81	0	0	0	0	0	0.39	0.33	0.22	0.08	0.08
CA corn	3.81	0	0	0	0	0	*0.08*	0.07	0.05	0.02	0.02
MS soybean	1.91	0.03	0.02	0.02	0.01	0.01	0.46	0.40	0.28	0.11	0.10
CA corn	1.91	0.01	0.01	0.01	<0.01	<0.01	0.24	0.21	0.16	0.06	0.06
MN sugarbeet	1.27	0.27	0.25	0.19	0.08	0.08	0.64	0.55	0.42	0.18	0.18
CA sugarbeet	1.27	0.54	0.50	0.41	0.18	0.18	*1.35*	1.24	1.02	0.45	0.45
TX wheat	2.54	0	0	0	0	0	1.08	0.86	0.60	0.22	0.22
CA wheat	2.54	0	0	0	0	0	0.34	0.30	0.25	0.12	0.12
Foliar (all)	--	--	--	--	--	--	0.4-11.4	0.4-11.4	0.3-10.9	--	--
Soil (all)	--	--	--	--	--	--	0.4-16.8	0.31-16.7	0.25-16.0	--	--

*Pore water concentration

In conclusion, incorporation of the new EFED approach for aquatic modeling of granular and treated seed applications is appropriate and will continue in future assessments of the neonicotinoids. In general, the revised methodology should better represent what happens in the field (*i.e.*, runoff of pesticide will occur, even when incorporated below 2 cm) and, while the EECs for incorporated products will change, overall these EECs are less than those for foliar and soil uses. As previously mentioned, additional updates to the aquatic invertebrate RQs are provided in a separate memo that summarizes the review and integration of new acute and chronic invertebrate data published by Raby *et al.* in 2018[5].

[5] Raby, M; Nowierski, M.; Perlov, D; Zhao, X.; Hao, C; Poirier, D.G. and P.K. Sibley. 2018a. Acute Toxicity of 6 Neonicotinoid Insecticides to Freshwater Invertebrates. Environmental Toxicology and Chemistry, 37 (5): 1430–1445. MRID 50776401.
Raby, M; Zhao, X.; Hao, C.; Poirier, D.G. and P.K. Sibley. 2018b. Chronic toxicity of 6 neonicotinoid insecticides to Chironomus dilutus and Neocloeon triangulifer. Environmental Toxicology and Chemistry, 37 (10): 2727-2739. MRID 50776201.