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MEMORANDUM

SUBJECT: Environmental Fate and Effects Division (EFED) Response to Public Comments on the Proposed Interim Decision (PID) for Acetamiprid

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This document provides the Environmental Fate and Effects Division (EFED) response to public comments received on the Proposed Interim Decision (PID) for Acetamiprid[1] (USEPA, 2020, EPA-HQ-OPP-2012-0329). Comments relevant to EFED are related to the Registration Review ecological risk assessment (USEPA, 2017, DP Barcode 441940; USEPA, 2020, DP Barcode 447655) and drinking water exposure assessments (USEPA, 2017, DP Barcode 441939). EFED responded to comments specific to acetamiprid received from Nisso America Inc. on behalf of the technical registrant Nippon Soda Co., Ltd (EPA Company Number 8033; referred to as Nisso) and from an anonymous commenter. Several comments were submitted to dockets that involve several neonicotinoid pesticides, including acetamiprid. Comments applicable to

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neonicotinoids in general are being addressed in a neonicotinoid general response to comment document (USEPA, 2021, DP Barcode 460138) and are not discussed in this document.

EFED appreciates the comments and careful consideration of the acetamiprid Registration Review work. Nisso's comments (Docket ID EPA-HQ-OPP-2012-0329-0103) related to clarification on toxicity endpoints and label mitigation recommendations. EFED clarified the toxicity endpoints; however, these comments and subsequent clarifications did not influence/alter risk conclusions. An anonymous commenter (Docket ID EPA-HQ-OPP-2012-0329-0141) noted data deficiencies and expressed concerns on whether the proposed mitigations were adequate to prevent potential risks to various taxa. EFED recommends an updated pollinator hazard statement based on the public comments (see comment 4 for details). EFED defers to PRD on the recommended label mitigations and whether potential risk concerns are adequately addressed considering risk and benefits. Overall, comments summarized in the neonicotinoid general response to comments document did not impact the risk conclusions already summarized for acetamiprid.

Below comments from the public are summarized and EFED responses are provided.

1. **Nisso Comment, Acute Freshwater Toxicity Endpoint:** *"The endpoint for acute toxicity to freshwater invertebrates of 3.31 µg/L was applied to the aquatic risk assessment in the PID. However, in the Preliminary Risk Assessment (PRA) for acetamiprid, the most sensitive acute endpoint was a LC50 value of 0.0209 mg a.i./L from the study report, Putt, A. (2003) Acetamiprid Technical--Acute Toxicity to Midge (Chironomus riparius) Under Static Conditions, which concluded the LC50 value of 0.024 mg a.i./L (MRID 45916201). Therefore, 0.0209 mg a.i./L concluded in the PRA should be used for the acute risk assessment."*

EFED Response: While the *Preliminary Environmental Fate and Ecological Risk Assessment in Support of the Registration Review of Acetamiprid (PRA)* indicates that the most sensitive freshwater aquatic invertebrate 48-hour median lethal concentration (LC_{50}) is 0.021 mg/L (21 µg/L; MRID 45916201) in **Table 23** (USEPA, 2017, DP Barcode 441940), this endpoint was updated in subsequent analysis described in the *Response to Public Comments and Update to the Preliminary Environmental Fate and Ecological Risk Assessment for Acetamiprid* (USEPA, 2020, DP Barcode 447655). The updated toxicity endpoint is documented in **Table 1** of the response to comments document as 3.31 µg/L (MRID 50776401), which matches the value cited in the PID.

2. **Nisso Comment, Chronic Freshwater Invertebrate Toxicity Endpoint:** *"The PID determined the freshwater invertebrate chronic toxicity endpoint was NOAEC = 0.36 µg a.i./L. This NOAEC value was derived from the results of a public domain report (Raby et al. (2018)). In this public domain report, almost all endpoints with acetamiprid showed "poor" or "no" concentration-response relationship except for the % complete emergence and % survival at 14-days. The concentrations of the test solutions were analysed by LC-MS/MS; however, the*

analytical method validation such as recovery rates, matrix effect, stability linearity, etc. was not conducted and the details of the methods were not given. Therefore, it is possible the measured concentrations were underestimated due to measurement error. Hence, neither the observation results nor the measured concentrations are considered reliable....

Conversely, Nisso submitted a chronic toxicity study with C. riparius (McElligott, A. (1999) Acetamiprid: Toxicity to the Sediment Dwelling Chironomid Larvae (Chironomus riparius) - 28 Days) that was conducted according to GLP regulations (MRID 50643901). ...The Nisso GLP study has not been reviewed completely by EPA at this time. Therefore, we respectfully suggest the Agency continue to review this GLP study and apply the resulting NOEC of 5 µg/L to the aquatic risk assessment for acetamiprid."

EFED Response: As noted in the response to comments (DP Barcode 441940) on the preliminary risk assessment of acetamiprid, new data on the toxicity of acetamiprid to freshwater benthic invertebrates are now available to the Agency from two newly published papers (Raby, Nowierski, *et al.*, 2018; Raby, Zhao, *et al.*, 2018) listed below.

> Raby, M., Zhao, X., Hao, C., Poirier, D. G., & Sibley, P. K. 2018. Chronic toxicity of 6 neonicotinoid insecticides to Chironomus dilutus and Neocloeon triangulifer. *Environmental Toxicology & Chemistry, 37*(10), 2727-2739. ECOTOX No. 395387; MRID 50776201.
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> Raby, M., Nowierski, M., Perlov, D., Zhao, X., Hao, C., Poirier, D. G., et al. 2018. Acute toxicity of 6 neonicotinoid insecticides to freshwater invertebrates. *Environmental Toxicology and Chemistry, 37*(5), 1430-1445. ECOTOX No. 392452, MRID 50776401.

Briefly, in the PRA an acute 48-hour LC_{50} value of 21 µg ai/L for *C. riparius* was used based on available registrant-submitted data (MRID 45916201). Chronic toxicity data for freshwater invertebrates were not available for the PRA, and so an acute-to-chronic ratio (ACR) based on available data on the estuarine/marine mysid shrimp (*Americamysis bahia*) were used to estimate a No Observable Adverse Effect Concentration (NOAEC) of 0.8 µg ai/L for midge. On the basis of the new acute toxicity data (Raby, Nowierski, *et al.*, 2018), an empirical 96-hour LC_{50} value of 3.31 µg ai/L for *C. dilutus* is now available. On the basis of the new chronic toxicity data (Raby, Zhao, *et al.*, 2018), a 20-day NOAEC value of 0.36 µg ai/L for *Chironomus dilutus* was identified based on 47 and 15% reductions in percent of emerged adults and average days to emergence, respectively, at the Lowest Observable Adverse Effect Concentration (LOAEC) of 0.71 µg ai/L. The actual studies are more thoroughly discussed in the previous response to comments. While there was not a consistent dose response for some acetamiprid endpoints, there was a reliable dose-response relationship for the toxicity endpoint identified in the PRA response to comment analysis (USEPA, 2020, DP Barcode 447655). Additionally, toxicity data across available information for acetamiprid suggest that the 0.36 µg/L NOAEC utilized in the

most recent response to comments analysis, is near concentrations where effects may occur for acetamiprid. This endpoint is supported by:

- the NOAEC for *Neocloeon triangulifer*[2];
- the NOAEC observed for *chironomus dilutus*[3]; and,
- an acute-to-chronic ratio (ACR) estimated value for the *Chironomus riparius* (ACR estimated NOAEC for midge = 0.8 µg/L).

Finally, it is reasonable to have some inter-laboratory variability in measured toxicity endpoints (Burton Jr. *et al.*, 1996; USEPA, 1984) and it is probable that the most sensitive aquatic invertebrate has not been tested. The weight of evidence across aquatic invertebrate toxicity data for acetamiprid indicates the value utilized to calculate RQs is within the range where chronic effects to aquatic invertebrates may occur and is considered reliable for the risk assessment.

Regarding the concern for the missing details on the analytical methods, EFED considers these details important but in this case the uncertainty resulting from this is small. In EFED's open literature review of Raby *et al.* (2018), both the measured and nominal concentrations are summarized in **Table 3**, **Table 4** and **Table 8**. While some detailed information on the methods is not fully summarized, information is available on recoveries and the difference between the measured and nominal toxicity endpoints is small (0.36 µg/L measured[4] versus 0.50 µg/L nominal) and would not have a substantial impact on the risk assessment. This level of difference is commonly observed in toxicity studies.

3. **Nisso Comment, Pollinator Data Requirements:** "*On page 14 of the PID, the Agency states, "...the EPA is currently determining whether additional pollinator data are needed for acetamiprid" and "The pollinator studies that could be required are listed on Table 1." Nisso respectfully reminds the Agency that we previously submitted numerous pollinator studies (both Apis and non-Apis) including "Tier 1" acute and chronic toxicity studies with adults and larvae as well as several "Tier 2" semi-field studies. We believe the existing data on-hand at the Agency are sufficient for regulatory purposes and no further data are needed to conduct risk assessments."*

   Anonymous Comment, Pollinator Data Requirements: "*Although there are several outstanding pollinator studies that need to be submitted to EPA to fully assess risk to*

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[2] NOAEC/LOAEC = 0.50/1.0 µg/L nominal; 82% decrease in survival to PEN and 85% decrease in survival to adult

[3] NOAEC/LOAEC = 0.50/1.0 µg/L nominal; 47% decrease in percent emerged and 15% change in days to emergence

[4] As summarized in the PRA response to comments document, samples of the test solutions from the nominal 0.25, 0.5 and 1 µg ai/L treatment levels were analytically verified twice during the study, with measured concentrations averaging 71% of nominal concentrations. The measured concentration was extrapolated based on average recovery and there is some uncertainty in those measured values.

pollinators from exposure to acetamiprid, the agency is not asking for these studies at this time."

EFED Response: As stated in the PID, this is simply a list of studies that could be required, if additional data are determined to be needed. The honey bee (*Apis mellifera*) data and terrestrial invertebrate risk assessments are fully described in the PRA (USEPA, 2017, DP Barcode 441940), PRA response to comments (USEPA, 2020, DP Barcode 447655) documents, and Data Evaluation Records (DERs) completed for the honey bee studies. However, as noted in the earlier response to comments (DP Barcode 441940) on the preliminary risk assessment, additional data have been submitted to the Agency since the PRA was completed that allow for enhancement of EFED's risk estimation presented in the 2018 ecological risk assessment. Briefly, in the PRA an acute LD_{50} value of 21.73 µg ai/larva based on data from the available 7-day repeat dose study (*i.e.*, chronic toxicity study; MRID 50015703) was used, along with the NOAEL value (*i.e.*, 12.2 µg ai/bee) from the same study; however, this study did not extend through adult emergence and was therefore classified as supplemental. In an addendum to the data evaluation record, the NOAEC/LOAEC were revised to <37.7/37.7 mg ai/kg-diet and NOAEL/LOAEL of <5.87/5.87 µg ai/larva (DER amendment 1/10/2020).

In the newly submitted acute (single dose) larval toxicity study (MRID 50581901), acetamiprid has a 72-hour LD_{50} value of 1.16 µg ai/larva. In the newly submitted 22-day larval chronic toxicity study (MRID 50581902), there was a 29% decrease in cumulative survival at the LOAEL of 0.35 µg ai/larva/day, resulting in a NOAEL value of 0.12 µg ai/larva/day. Therefore, the full suite of pollinator Tier I laboratory-based acute and chronic toxicity data on adult and larval bees is available for acetamiprid, although there are some uncertainties in whether the test material was representative of products registered in the United States for adult acute contact toxicity study (OCSPP 850.3020). Tier I data analysis indicate that both acute and chronic risk Levels of Concern (LOCs) are exceeded for adult and larval *Apis* and non-*Apis* bees.

The draft risk assessment and EFED's response to comments received on the draft risk assessment both acknowledge that higher-tier studies have been submitted. While the colony-level studies do not indicate adverse effects to the colony, these studies were conducted at application rates at or below 0.15 lb ai/A, which is less than the maximum single application rate of 0.52 lb ai/A allowed on labels for ornamentals.

The registrant is correct in noting that residue data have been provided for pollen and nectar (MRID 50015701). These data were collected as part of semi-field studies (OECD Guidance Document 75) and indicate that measured residues were 70 – 99% lower than those predicted in BeeRex for the corresponding application rate; however, residues measured in the studies were high enough to exceed some of the laboratory toxicity endpoints. As noted in the draft risk assessment, there is uncertainty regarding the extent to which the formulation of acetamiprid used in the studies is representative of products registered in the U.S. and their maximum application rates. Also, rain events during the study may have affected the extent to

which bees may have been foraging as well as the extent to which acetamiprid was available for uptake/distribution by the plants.

The draft risk assessment also reports on acute oral and contact toxicity of formulated acetamiprid to the non-*Apis* social bee *Bombus terrestris*; however, there is uncertainty regarding the extent to which the formulation tested reflects the toxicity of acetamiprid formulations currently registered for use in the U.S. In general, there is uncertainty whether impact to colonies may occur at the maximum application rates for acetamiprid. As described in the risk assessments, there are incidents associated with the use of acetamiprid and bees; although very limited information is available on the incidents.

EFED has accounted for the available Tier 1 data for quantitatively assessing risk to bees and has identified the available higher-tier data for qualitatively refining risk estimates. As part of the characterization of available data, EFED has also articulated the uncertainties. Risk managers are considering whether the uncertainties in the terrestrial invertebrate risk assessment indicate additional data are needed.

4. **Nisso Comment, Proposed Pollinator Labeling Changes:** "*A sentence in the Agency's proposed pollinator advisory language reads: "This product is moderately toxic to bees and other pollinating insects exposed to direct treatment, or to residues in/on blooming crops or weeds." Nisso is proposing to delete text in the sentence related to residues in/on blooming crops or weeds since the Agency states on page 14 of the acetamiprid PID"* In summary, Nisso indicates that as the agency states that measured residue data suggest lower EECs than those used to generate RQs and colony-level studies suggest that effects are transitory, the hazard statement should be modified.

   Anonymous Comment, Proposed Pollinator Labeling Changes: "*The proposed interim decision also included an environmental hazard statement on labels for pollinators, indicating that acetamiprid is moderately toxic to bees, but does not mention high toxicity to larvae*"

EFED Response: Pollinator hazard statements are recommended based on Chapter 8 of the Label Review Manual (USEPA, 2018). As noted in the preliminary risk assessment, acetamiprid is classified as moderately toxic to adult bees based on an acute contact LD_{50} of 10.5 µg a.i./bee (MRID 50015704), placing the chemical in Toxicity II as specified in the Label Review Manual. However, given the results of the toxicity of residues on foliage study (850.3030) with a residual toxicity time for 25% bee mortality (*i.e.*, RT25) of less than 3 hours, no extended residual toxicity statement is triggered. EFED defers to PRD on the final recommended pollinator hazard statements.

5. **Nisso Comment, Proposed Vegetative Filter Strip:** *"Nisso's acetamiprid product labels for ASSAIL 70 WP (EPA Reg. No.8033-23) and ASSAIL 30 SG (EPA Reg. No. 8033-35) currently*

contain the following statement: "Do not cultivate or plant crops within 10 feet of aquatic areas as to allow growth of a vegetative filter strip." For parity with other product labels requiring vegetative filter strips around aquatic areas, we are proposing that the aforementioned filter strip statement be followed by: "Western irrigated agriculture is exempt from this requirement. Western irrigated agriculture is defined as irrigated farmland in the following states: WA, OR, CA, ID, NV, UT, AZ, MT, WY, CO, NM, and TX (west of I-35)."

EFED Response: EFED understands that vegetative filter strips (VFS) may not be possible in many areas in the Western United States. In some registration review cases, alternative mitigations were applied in place of the VFS in these areas. EFED defers to Pesticide Re-evaluation Division (PRD) on this label recommendation.

6. **Anonymous Comment, Recommended Label Mitigation and Availability of the Final Assessment:** The anonymous commenter summarized some of the risk conclusions of the ecological risk assessment, noted several data deficiencies in the evaluation and generally indicated that the recommended mitigations did not eliminate the potential for risk and were troubling, given some of the potentials for risks. Noted risk concerns include potential risk to pollinators, birds, terrestrial plants, and aquatic invertebrates. For birds, the commenter indicated it was unlikely that farmers would be able to prevent spillage or foraging for seed below the surface. The anonymous commenter indicated that there was a lack of a terrestrial risk assessment for soil-dwelling organisms. Finally, the commenter inquired on when a final risk assessment would be completed and shared with the public, and whether the public would have another change to provide feedback.

EFED Response: EFED appreciates the summary and concerns from the anonymous commenter. While no chronic data are available for passerine species of birds, there is not a standard test guideline for conducting a chronic toxicity study on passerines. Thus, conducting such a study may not be possible and would require method development. However, chronic toxicity data are available for both Mallard Ducks (*Anas platyrhynchos*) and Northern Bobwhite Quail (*Colinus virginianus*). Based on a NOAEC of 99 mg ai/kg diet, chronic LOC exceedances are already identified for birds, and requiring additional data for small birds is not expected to change the risk conclusion. EFED noted this uncertainty in the PRA.

With respect to pollinators and as indicated in response to an earlier comment, the full suite of acute and chronic toxicity studies are available for adult and larval bees. Also, higher-tier studies including measured residues in pollen and nectar as well as both semi-field and full-field colony-level studies have been considered. While there are some deficiencies in the pollinator studies, the current data available are quite robust. The weight of evidence suggests that the likelihood of long-term colony-level effects of acetamiprid is low up to 0.089 lbs a.i./A; however, both the preliminary risk assessment and the earlier response to comments on the preliminary risk assessment indicate uncertainties regarding potential risks at higher application rates. While uncertainties still exist in the data, the risk and benefits of the use of acetamiprid

must be considered in determining whether additional data are needed. EFED defers to PRD on whether additional data are needed to resolve these uncertainties.

While EFED does not currently have a standard methodology to assess risk to soil-dwelling organisms in EFED, this is a relevant concern for pesticide risk assessment; methodologies are in development and undergoing harmonization within the ecotoxicology field (EFSA *et al.*, 2017; Jänsch *et al.*, 2006; Römbke *et al.*, 2018). Currently, EFED summarizes available data on terrestrial invertebrates in risk assessments and effects on reproduction and emergence in some studies of acetamiprid degradates are described in **Appendix B** of the PRA for acetamiprid.

EFED defers to PRD on the concerns expressed by the anonymous commenter on whether the proposed mitigation is appropriate given the potential risk and benefits of the use of acetamiprid. However, the preliminary risk assessment evaluates the potential risk to both birds and mammals from the consumption of treated seeds under the assumption that a percentage of the seeds will remain sufficiently close to the surface to be available for consumption. The assessment also assumes though that the animal's entire diet will consist of treated seed, which is a conservative assumption and is intended to protective. While the proposed mitigation is not likely to completely eliminate exposure to birds and mammals to treated seed, it may help reduce the potential for exposure.

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