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WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: **Mancozeb:** EPA Response to Comments Related to Mancozeb: Draft Ecological Risk Assessment for Registration Review and Mancozeb: Drinking Water Assessment to Support Registration Review (EPA HQ-2015-0291- 0023).

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This memorandum transmits the Agency's responses to public comments received on the Environmental Fate and Effects Division's (EFED) Draft Ecological Risk Assessment [1](ERA) and Drinking Water Assessment [2](DWA) to Support Registration Review. Comments were

[1] December 16, 2020. Mancozeb: Draft Ecological Risk Assessment for Registration Review.
[2] December 10, 2020. Mancozeb: Drinking Water Assessment to Support Registration Review.

received from several entities including the Mancozeb Task Force (technical registrants) and other governmental and non-governmental entities. Comments and the Agency's responses relative to the ERA/DRA are listed below. The specific commentors addressed are listed below with the parenthetical abbreviation noting how they are referred to in this document:

- Center for Biological Diversity (CBD),
- Mancozeb Task Force [3](MTF),
- National Agricultural Aviation Association (NAAA),
- United States Department of Agriculture (USDA), and
- UPL NA Inc. / UPL Delaware, Inc. (UPL).

I. Center for Biological Diversity (CBD) Comments

(1) Comment: *Risk to Terrestrial Invertebrates:*

a) The Draft Ecological Risk Assessment (DRA) found risk quotients (RQs) exceed the level of concern (LOC) on a chronic basis to honeybee larva. Mancozeb presents significant risk despite several data gaps including: no adult chronic toxicity endpoint, no data on the contamination of nectar and pollen, and no quantitative tier II or III assessment for pollinators. Additionally, the tier II study cited showed "no sustained impact" at the colony level. We do not agree that this tier II assessment is adequate to capture the sublethal effects to terrestrial invertebrates. This lack of toxicity information based on multiple endpoints hamstrings the risk assessment from being able to show a complete picture of risk to terrestrial invertebrates besides the honeybee.

b) The EPA wholly and completely relies on honeybees as the surrogate for all terrestrial invertebrate species which perpetuates an ignorance of the life history and exposure pathways of non-apis bees and other invertebrates. Non-apis bees have exposure pathways that are different than honeybees primarily in their increased contact with soil, social structure, and differences in feeding habits. The vast majority of native bees are solitary and ground-nesting which has many implications for the exposure of these bees to mancozeb.

Furthermore, the persistent residues of pesticides in soil can contaminate bumble bee nests and overwintering sites, but this is not considered by the EPA when assessing risk of pesticides to bumble bees.

c) EPA has broad discretion to compel the registrant to provide additional data in order to "incorporate multiple lines of evidence and alternative exposure scenarios into the risk description." EPA can address gaps in their risk analysis by compelling the registrant to conduct studies on the toxicity of mancozeb to the blue orchard mason bee (Osmia lignaria)

[3] Group of technical registrants comprised of UPL and Corteva

and to the alfalfa leaf cutter bee (Megachile rotundata). The EPA can use these additional test species to estimate exposure through routes other than nectar and pollen. The mason bee uses mud to partition between nesting cells and therefore can identify the risks to bees and other soil-dwelling invertebrates from the long-term, chronic exposure to mancozeb and its degradation products in contaminated soil. The alfalfa leaf cutter bee females use leaves to line the inside of their brood cells. This bee's larvae and adults are exposed for long periods of time to direct contact with leaves that contain mancozeb residues and would serve as a better, but not complete proxy for terrestrial invertebrates that consume or are in direct contact with vegetation throughout part or all of their life cycle. Toxicity data from soil and vegetation exposure would also help provide information on the possible harms to beneficial non-target insects that serve as biological controls for pest species.

EPA Response:

In response to bullet (a), EFED indicates that the only data gap in the Tier 1 bee toxicity dataset for mancozeb pertains to the chronic adult oral toxicity study for honey bees. This study was classified as being suitable only for qualitative use in risk assessment because test concentrations were not analytically confirmed. However, as indicated in the draft ecological risk assessment, chronic risk to adult bees is suggested for the higher use rates of mancozeb based on nominal concentrations from this study. In accordance with the Office of Pesticide Programs (OPP) *2014 Guidance for Assessing Pesticide Risks to Bees*, the need for higher tier studies of bees does not solely depend on the findings from lower tier risk assessment. Rather, the need for higher tier data also depends on risk management considerations, including the ability to mitigate risks identified at lower tiers, factors related to balancing risks vs. benefits of registered uses, and the expected impact a new study would have on these considerations. Since these risk management considerations have yet to be determined by OPP, the need to require additional higher tier data has not been finalized. Once all risk assessment and risk management factors are fully considered, OPP will determine appropriate risk mitigation measures and potential need for additional data.

In response to bullet (b), EPA relies on the honey bee as a surrogate species as outlined in the 2014 bee risk assessment guidance and 2012 pollinator white paper. While EFED acknowledges there are limitations to this approach, the surrogate approach is consistent with the general risk assessment methodology used for all taxa in EPA's FIFRA risk assessments. To assess the state of science associated with exposure of *non-Apis* bees to pesticides, EPA helped convene a workshop[4] in 2017of experts in the ecology and biology of non-*Apis* bees. EPA notes that the conclusions of the 2017 non-*Apis* bee exposure workshop indicated that the honey bee is a reasonable surrogate for non-*Apis* bee exposure via pollen and nectar due to its comparatively high consumption rates of these matrices. As for exposures via soil and leaves, EPA concurs with the workshop findings that the honey bee life history is not representative of potential

[4] Boyle, N. K., Pitts-Singer, T. L., Abbott, J., Alix, A., Cox-Foster, D. L., Hinarejos, S., Lehmann, D. M., Morandin, L., O'Neill, B., Raine, N. E., Singh, R., Thompson, H. M., Williams, N. M., & Steeger, T. (2018). Workshop on Pesticide Exposure Assessment Paradigm for Non-Apis Bees: Foundation and Summaries. *Environmental Entomology*, *48*(1), 4–11. https://doi.org/10.1093/ee/nvy103

exposure of non-*Apis* bees via soil (*e.g.,* ground nesting bees) and leaf surfaces (*e.g.,* leaf cutting bees). However, as concluded by workshop participants, data are insufficient to quantify exposure of non-*Apis* bees from these routes. Specifically, additional research is needed to quantify the dependency of exposure on species-, chemical- and matrix-specific factors related to soil and leaf exposure matrices. Once such data are generated, then comparative risk assessments can be done to document the extent to which risks to honey bees (contact and pollen/nectar consumption) are indicative of risks to non-*Apis* bees via these other exposure routes.

In response to bullet (c), it is the purview of the risk management team whether to request additional data if the provided assessment is not sufficient or guidelines have not been met. The decisions to require data does not solely depend on scientific uncertainty. It also depends on other considerations of risk management, including the ability to mitigate risks, availability of pesticide alternatives, balancing risks with associated benefits of registered uses, and the expected impact a new study would have on these considerations. At this time, these and other factors are being actively considered for mancozeb. Once decided, OPP will publish this information for public comment as part of OPP's Preliminary Interim Decision (PID) for mancozeb.

(2) Comment: *Harms to Beneficial Fungi:*

a) EPA's risk analysis does not consider the topic of beneficial fungi at all. EPA did not compel the registrant to provide any information about the toxicity to beneficial fungi and consequently cites no toxicity studies and calculated no risk quotients for beneficial fungi. Yet, an independent study of arbuscular mycorrhizal fungi (AMF) found them to be sensitive to mancozeb at all doses tested with effects likely at <10ppm in soil. Mancozeb has a IC_{50} of 5.6ppm for the AMF Gigaspora albida.

EPA Response:

The Agency does not currently consider risk to fungi when analyzing risks to non-target taxa and toxicity data on fungi are not included in the Agency's data ecological effects data requirements outlined in 40 CFR Part 158 Subpart G. While EPA is aware that certain fungi provide beneficial functions to plant and ecosystem health, standard methods for quantifying pesticide effects on such fungi are not available at this time. Lack of such standardized methods greatly limits the Agency's ability to conduct risk assessment of fungi. The Agency further notes that agricultural soils are highly managed systems that undergo considerable physical and chemical (non-pesticide) alteration designed to optimize crop production. Since these soil alterations themselves may also impact beneficial fungal structure and function in agricultural systems, any consideration of pesticide risks to fungal communities would need to be evaluated in the context of these other potential stressors.

(3) Comment: *Lethality Is Not a Suitable Endpoint for an Endocrine Disrupting Fungicide:*

Mancozeb is known to cause multiple sublethal harms to a variety of wildlife which clearly impair development and reproduction. Chronic toxicity endpoints are essential to understanding the full risk of the use of mancozeb and to produce effective mitigations that lower risk. The lethal endpoint is often the least sensitive to pesticide toxicity even though they are the most studied. Impacts at the molecular, genetic, and cellular level produce additional bioindicators that are more sensitive to the effect of a pesticide like mancozeb that is unlikely to cause acute toxicity.

Based on EPA's DRA and other pesticide risk assessments, EPA is aware that many fungicides cause sublethal effects. However, they choose not to analyze the impacts that fungicides clearly have to foraging bees and terrestrial invertebrates. EPA must have substantial evidence to re-register this pesticide and must require all necessary data and studies, including, but not limited to any previously identified data or study gaps, additional studies to evaluate effects on pollinators in accordance with the Guidance for Assessing Pesticide Risks to Bees, information concerning endocrine disruption effects, and any information that this pesticide or products containing this pesticide may have synergistic effects. Failure to require any of the above information will result in the EPA underestimating adverse effects and lacking substantial evidence to support registration.

EPA Response:

EFED reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. These studies include endpoints which may be susceptible to endocrine influence, including effects on sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. EFED reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. For mancozeb the most sensitive chronic endpoint for mammals was growth, expressed as body weight gain. To the extent that endocrine mediate effects are expressed in these and other apical endpoints, EPA's ecological risk assessment would incorporate these effects. In addition, EPA has developed the endocrine disruptor screening program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Additionally, where reliable data are available, EPA does evaluate co-formulated products (co-formulated with multiple a.i.s) or typical end-use products (with one or multiple a.i.s) independently if there is evidence of synergistic effects for these products than for the individual technical grade a.i.

(4) Comment: *The EPA Must Take into Account Real-world Scenarios:*

The EPA often claims that it is acting conservatively by using the maximum labeled use rates when estimating exposure to plants and animals. These upper-level exposure scenarios, however, do not take into account accidental spills and illegal uses of the pesticide. An

assumption of 100 percent label compliance underestimates risk and is unsupported by state-collected data.

Ever-present possibility of an accidental spill, label misunderstanding, or improper disposal indicates that this is a reasonably foreseeable event that should be accounted for when estimating peak exposure concentrations. In addition, the data that are available on label compliance indicate that it is unreasonable to assume that pesticides are always applied in accordance with the label. We feel that when communicating findings to a risk manager, the EPA should no longer refer to its use of maximum labeled rates as "conservative" or accurately estimating peak exposures that may occur.

EPA Response:

In evaluating a pesticide registration application, in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the EPA assesses a wide variety of exposure information (i.e., where and how the pesticide is used) and studies concerning environmental fate (i.e., how the chemical will move in the environment) and toxicity (i.e., effects on humans and other non-target organisms) to determine the likelihood of adverse effects (i.e., risk) from exposures associated with the labeled uses of the product. However, the scenario involving exposures due to accidental spill, label misunderstanding, or improper disposal are substantially different than the scenarios typically evaluated when assessing ecological risks based on the use of a compound as specified on the product label. Since there are multiple ways in which pesticides in general can be misused or disposed of, and while some labels may specify restrictions, FIFRA dictates that ecological risks are evaluated in terms of exposures that are a result of the application rates and not improper or illegal use.

(5) Comment: *The EPA Must Assess the Enhanced Toxicity of Pesticide Mixtures:*

Fungicides are very often mixed with other pesticides when applied. The mixture of pesticides applied at one time and over subsequent growing seasons increases the cumulative amount of pesticide present in the environment which exceeds risk thresholds that are not accounted for in the DERA. Mixtures and end-use products contain more ingredients than the single active ingredient analyzed in the DRA, and the combination of ingredients can have the effect of increasing toxicity. For example, mixtures of fungicides and certain other pesticides are known to have acute synergistic effects by greatly increasing the toxicity of the insecticide. Mancozeb can also interact with other pollutants and increase sensitivity to the fungicide. To be compliant with FIFRA, the EPA must do an analysis of mixture toxicity with mixtures containing this active ingredient before any registration decision can be made.

EPA Response:

While EPA recognizes that organisms may be exposed to pesticide mixtures, its ability to quantify risks from such mixtures is limited by lack of reliable methods and data to predict exposure levels and responses to the myriad of potential pesticide mixtures. Available data on

the toxicity of mixtures indicate that the toxicity of a chemical mixture can vary by many factors, including the relative quantities of each mixture component. Additionally, the large number of unique combinations of pesticide mixtures makes predicting exposure and effects of each of these combinations impractical. Where reliable data are available, EPA does evaluate co-formulated products (co-formulated with multiple a.i.s) or typical end-use products (with one or multiple a.i.s) independently if there is evidence of greater toxicity for these products than for the individual technical grade a.i.

II. Mancozeb Task Force (MTF) Comments

(1) Comment: *Residues of Concern:*

While EBIS, ETU and EU are considered the major products/metabolites of parent mancozeb degradation, inclusion of these in the mancozeb residues of concern ROC) term is not appropriate because of the low relative toxicity of these metabolites compared to parent mancozeb. With regard to EU, EDA and HYD, these metabolites constitute minor degradates and therefore should not be considered in the ROC term. UER by definition are un-extractable residues and therefore have minimal potential for exposure to aquatic and terrestrial organisms. The low potential for adverse effects to sediment dwelling organisms, the principal deposition compartment of eroded UER has been demonstrated (Hughes, 2018; MRID 47410102).

EPA Response:

The residues of concern for mancozeb ***did not*** include *EU, EDA, HYD* and the un-extractable residues. In regard to aquatic exposure, *EU, EDA, HYD* degradates were not considered of concern because they were minor degradates or because toxicity information was available showing less toxic concern. In the terrestrial exposure, all but EU were not considered as residues of concern.

(2) Comment: *Residues of Concern:*

As noted previously, the inclusion of the metabolites EBIS, ETU, EU and EDA, whether formed in soil or the aquatic compartment in the mancozeb ROC term is not appropriate because of the low relative toxicity of these metabolites compared to parent mancozeb. With regard to the sediment organism toxicity of the UER, a sediment organism toxicity study has been conducted and submitted and has demonstrated that the UER is indeed un-extractable and has been shown to exhibit negligible toxicity to sediment dwelling organism (Hughes (2018) (MRID 47410102)).

EPA Response:

As a result of mancozeb rapid degradation, early intervals in the environmental fate studies submitted for mancozeb determined either EBIS alone or mancozeb and EBIS to be present immediately. Therefore, it was necessary to assume that mancozeb and its transformation product EBIS as parent for all of other degradates in order to calculate the necessary half-lives for modeling. As mentioned before (item 1, above), the residues of concern for mancozeb ***did not*** include *EU, EDA, HYD* and the un-extractable residues.

(3) Comment: *ETU:*

USEPA has noted (Table 5.6 in the Draft Ecological Risk Assessment for Registration Review document) that ETU is stable to hydrolysis and phototransformation in sterile aqueous solutions and soil media. However, sensitizers in natural waters and likely in soil pore water will result in rapid indirect photolysis of ETU via a catalyst process. The aquatic photolysis study (Carpenter and Fennessey, 1987; MRID 40466102) provides the best t1/2 in aqueous solutions; 2.3 d for sensitized exposed treatment.

EPA Response:

EFED concurs with MTF comments noting that stability of ETU in sterile aqueous photolysis was used for modeling and was derived from its weak absorption of light in the visible range with maxima between 290 to 310 nm. The DRA indicated that ETU may be susceptible to indirect aqueous photolysis in the natural environment.

(4) Comment: *Un-extracted Residue (UER):*

MTF has submitted un-extractable residues studies that have demonstrated that the nominal UER are indeed un-extractable. Additionally, a sediment dwelling organism toxicity study has been submitted and demonstrated that the UER exert limited or no potential for adverse effects to exposed sediment dwelling organisms (Hughes (2018) (MRID 47410102).

EPA Response:

UER was considered bound residues based on recently submitted exhaustive extraction procedures used in these studies. However, EFED pointed out the uncertainty associated with UER in studies submitted prior to the problem formulation, therefore the assessment of potential risk from UER was based on submitted sediment toxicity data.

(5) Comment: *Terrestrial Field dissipation:*

No acceptable terrestrial field dissipation studies are available for mancozeb as the chemical is believed to be non-persistent in field soils based on previously discussed data. Aerobic soil dissipation data supports such a conclusion especially when concentrations used are below the mancozeb solubility limit. In the field, single application to crops is expected to result in maximum concentrations below the solubility limit of mancozeb. At these concentrations, mancozeb is expected to be non-persistent as it will readily undergo solvolysis/hydrolysis and microbial degradation. In the literature, a dissipation half-life (DT50) of 3 days was reported for a silty clay loam soil under Philippine field conditions using soil column receiving natural rainfall (a total of 12" in 21 days). Mancozeb, based on carbon disulfide (CS2) residues, remained on the top 2.5 cm and no leaching was observed under the conditions of the experiment. Both ETU and

EU were the only degradation products identified; whereas, unextractable residues were not characterized, but accounted for 38-70% of the total residues.

EPA Response:

Comment is noted.

(6) Comment: *Foliar Dissipation Half-life Used in T-REX:*

a) *MTF is not in agreement with EFED when considering the default foliar DT50 value of 35 days for mancozeb. To refine the foliar dissipation DT50 value for mancozeb, the MTF reviewed the dislodgeable foliar residue (DFR) studies summarized in Appendix E of the EPA Occupational and Residential Exposure Assessment in Support of Registration Review (D459484, 12-14-2020) where DT50 values ranged from 8.1 to 35.4 days for mancozeb and 3.6 to 28.7 days for ETU.*

   Upon closer examination of EFED's assessment, In addition, the MTF reviewed the studies that were now considered invalid as compared to the 2005 assessment. In the process, three of the studies determined not appropriate are deemed valid by the MTF for calculating the half-lives.

   The Agency claims that MRID 42560201 is not recommended for use in risk assessment. This study is a supplement to MRID 41836902, which the agency also categorized as "not recommended for use in risk assessment" and presents the data from the Florida site of the three sites described in the original protocol for MRID 41836902.

b) *Half-lives were calculated for each of the three sites; California and Maryland from the report cited by EPA (S. Matthew Cairns, March 28, 1991) and Florida from the follow up report by Dr. Richard Honeycutt (April 10, 1992). The formula used is the formula currently used by EPA and the industry for this purpose; t1/2 = ln(2)/-k(slope). A table is presented below with mancozeb and ETU half-lives (Refer to table in the comments document).*

   Therefore, using the valid data, the 90th percentile values of 17.6 days for mancozeb and 17 days for ETU have been calculated according to USEPA calculation method. The half-life of mancozeb and ETU are less than the T-REX default value and considering the minor conversion rate, considering mancozeb only in the ROC on feed items is justified.

EPA Response:

In response to bullet (a), the referenced dislodgeable foliar residue studies are not suitable for calculation of a refined foliar dissipation half-life for use in ecological assessments because the Health Effects Divison (HED) deemed these studies to be not suitable for use in risk assessment (MRID 42560201 and 41836902). Based on current HED guidance, the study has been determined not acceptable due to issues with rainfall and the total leaf area sampled. HED

would need to revisit and update their DER classification before these studies can be used for calculation of a chemical specific half-life in EFED assessments.

In response to bullet (b), the default half-life is deemed suitable for the EFED assessment because there is not sufficient information to refine. However, even when modeled for birds and mammals as characterization with a 17.6 day half-life, there are still estimated. Additionally, the draft ecological risk assessment reported chronic risk to birds and mammals from a single mancozeb application irrespective of selected half-life.

(7) Comment *Terrestrial Vertebrate Ecotoxicology*:

a) *MTF does question the ecological relevance of the long-term mammalian toxicity endpoint considered by EFED. Currently, a NOEL of 6.95 mg ai/kg bw/d based on decreased body weight observed in a 2-generation rat study (MRID 41365201) is used in the DRAFT EFED assessment. Changes in body weight are quite normal in mammalian species and do not reflect impaired fitness, especially if the changes are within the normal range for the species concerned.*

b) *Based on the rapid excretion of mancozeb and its metabolites, animals that feed on mixed diets, coupled with the rapid degradation of mancozeb in the environment as shown in several residue trials, the chronic risk to mammals is not correctly represented in the current DRAFT EFED assessment. The ecologically relevant toxicity endpoint of 68.9 mg a.i./kg bw/d should be used in the risk assessment. Note that this value is based on the maximum test dose (LOEC > 68.9 mg a.i./kg bw/d), hence adverse effects on reproduction may not be noted until animals are exposed to much higher dietary rates.*

EPA Response:

In response to bullet (a), changes in body weight (growth) are a widely accepted biological and apical endpoint for use in ecological risk assessment in accordance with Agency policy[5]. Effects on growth may be indicative of a wide variety of chemical mechanisms of action and are considered important for organism and population fitness.

In response to bullet (b), standard testing methodology represents a chronic exposure to mammals. Within the chronic test excretion of mancozeb and its metabolites would still happen. Repeated exposure to mancozeb is possible in the environment. Even when considering the current LOAEC (68.9 mg a.i./kg bw/d) as the selected endpoint in modeling as characterization (as discussed in the draft risk assessment) there is still the possibility for chronic risk to mammals with RQs exceeding the LOC.

[5] https://www.epa.gov/risk/ecosystem-services-ecological-risk-assessment-endpoints-guidelines

(8) Comment: ***Terrestrial Invertebrate Ecotoxicology:***

Acute oral risk to adult bees was based on the 'non-definitive' endpoint and some slight LOC exceedances were noted. Chronic oral risk was based on the nominal (not analytically verified) endpoint and some slight LOC exceedances were noted. No apparent impact prevents the risk assessment from being conducted and concluding that the potential for acute oral or contact risk to adult bees is negligible.

The fact that the conservative Tier 1 BeeREX-estimated EECs are consistent with the nominal mancozeb residues in pollen and nectar and that both the field study and calculated risk assessment using BeeREX indicate a low potential for adverse effects to exposed colonies should be considered confirmatory. It is noteworthy, additionally, that after 40+ years of use of mancozeb as a fungicide on a variety of crops no or few in field incidences have been recorded further indicating that the potential for adverse effects to bee colonies is negligible.

EPA Response:

EPA notes in its risk assessment the LOC exceedances for mancozeb at the Tier 1 level for bees. EPA further notes that by design, the Tier 1 risk assessment scheme is conservative and used as a screen. Currently, higher tier data on exposure and risk to bees is considered limited in scope and quality. EPA agrees with the lack of reported ecological incidents to date with bees. However, lack of reported incidents does not equate to lack of risk due to underreporting and other confounding influences affecting the causal interpretation of ecological incident reports. All of these multiple lines of evidence will be considered by the Pesticide Re-Evaluation Division (PRD) risk management team when creating risk management decisions.

(9) Comment: ***Off-site Risks to Aquatic Invertebrates from Spray Drift alone:***

The risk assessment outcomes derived as a function of spry drift can be refined using higher tiered AgDrift™ analyses.

In order to refine the spray drift exposure estimates for applied mancozeb at rates of 1.2 and 4.8 lbs a.i./A, AgDrift™ simulations were performed using Tier III for aerial applications. The application rates of 1.2 and 4.8 lbs a.i./A represent a minimum and a maximum rate of aerially applied mancozeb. AgDrift™ was parameterized based on the information provided by the National Agricultural Aviation Association (NAAA) per mancozeb applications (see accompanying letter, NAAA to USEPA Docket Center RE: Registration Review Draft Risk Assessments; Docket ID: EPA-HQ-OPP-2014-0131, August 6, 2020). The table below illustrates the AgDrift™ Tier III parameters for aerial fixed wing applications (Refer to Table in the comment document).

EPA Response:

AgDRIFT™ is the currently approved model for evaluating potential spray drift from a pesticide application. The agency appreciates the additional information on application practices (both ground and aerial) and continues to work with industry to update and improve modeling methods to better reflect these practices. Modeling in the mancozeb exposure assessment is based on label instructions and in the absence of specific application requirements on the label, default assumptions are used. Additionally, the risk assessment provided outputs for risks associated with ground and aerial applications, which will allow risk managers to understand the range of risks associated with different application methods.

(10) Comment: *Terrestrial Organism Risk Assessment*

a) ***Dietary Items on the Treated Field:*** *Short grass, long grass and broadleaf plants other than the target crop are unlikely to be present in managed fields. Growers apply herbicides to managed fields to protect and enhance yield from nutrient-robbing and disease-harboring weeds. Therefore, the assumption of the exposure assessment that these plant types are exposed within a managed field to the full rate of application of mancozeb results in an excessive over-estimation of exposure. At best, low growing weeds that may have escaped herbicide control may be present in managed fields and receive an indirect exposure to spray residues that are not intercepted by the target crop foliage. The exposure assessment for weeds in the in-crop scenario could take into account a crop interception factor.*

b) *Mancozeb is known to rapidly degrade, with a foliar dissipation half-life of 17.6 days (90th %ile) as noted above in the discussion under Foliar dissipation. EFED's Preliminary Ecological Risk Assessment considered the default value of 35 days and focuses on the maximum residue values (upper-bound Kenega) that overestimate the chronic exposure. EFED's rational for using the default value was to account for ETU formation and decline, however, as discussed the half-life for ETU is identical to mancozeb at ~17 days. Once again, considering the T-Rex default value is overly conservative especially since as stated in the EFED assessment the residue of concern (ROC) is mancozeb parent only for terrestrial organisms; exposure to food items is expected to be from applied mancozeb in addition to low concentrations of ETU.*

c) *Besides the overly conservative assumptions from the T-Rex model, note that the risk assessment assumes no precipitation between applications. Given that mancozeb is shown to hydrolyze quickly, residues remaining on food items will be short lived due to potential interception of rainfall, ground fog and dew formation. Hence the risk from chronic exposure presented in the current EFED document does not accurately illustrate the potential chronic risk to birds and mammals.*

d) *It is also noted that refined assessments were not considered in the current EFED risk assessment. MTF therefore believe it is pertinent to present a higher tier mammalian risk assessment.*

Intrinsik, Ltd. used the Wildlife Pesticide Risk Assessment Model (WildlifePRAM) to conduct a refined probabilistic assessment for those use patterns that potentially posed a risk to mammals. The refined probabilistic assessment was conducted with representative focal mammalian species that frequent row crops and orchards (i.e., meadow vole, masked shrew, white-footed mouse, eastern cottontail, white-tailed deer) and included a range of diets and body sizes. The results from the refined probabilistic assessment indicated that risks, although modest, are highest for mammals that forage exclusively in apple orchards (an unrealistic scenario) compared to the other registered mancozeb use patterns.

With regard to avian species, higher tier modelling should be used further to refine the risk through the use of Terrestrial Investigation Model (TIM, version 3.0 beta) and the Markov Chain Next Productivity (McNest) models. The results of this study demonstrated that use of mancozeb in apples and potatoes does not pose an acute or chronic risk to birds. That no risks were found in the modeling exercise is consistent with the absence of observed adverse incidents for birds following labeled mancozeb applications despite decades of widespread mancozeb use.

EPA Response:

In response to bullet (a), plants other than the desired crop are found on managed fields and many are difficult to manage which is why they are still present on the field. There is also the possibility that plants present at the edge of field that could also receive full or close to full application by spray. Finally, EFED terrestrial model (T-REX) does not have a way to incorporate additional crop interception factor when calculating EECs.

In response to bullet (b), the purpose of EFEDs ecological risk assessment is to first determine a conservative (screening level) estimate of possible risk. Those risks may be further refined using additional data and/or assumptions which vary in the level of conservatism. Currently, there is insufficient data to refine the default foliar half-life for this chemical. Also, in the ROC section it states that the reason ETU is not a residue of concern for terrestrial organisms is because of modeling constraints with the current system rather than a lack of toxicity or exposure. "Terrestrial exposure to food items is expected from applied mancozeb in addition to low concentrations of ETU. EFED uses the T-REX model based on a 35-day half-life. The 35-day half-life assumption is also expected to account for ETU formation and decline. Despite the transience of mancozeb observed in the available data, the inability of T-REX to simulate multiple stressors is conservatively offset by this 35-day default half-life assumption."

In response to bullet (c), EFED ecological modeling does not take into effect specific rain events for terrestrial EEC calculation, it uses "theoretical decline curves" to calculate exposure which do consider weathering.

In response to bullet (d), within the risk management decision-making process the Pesticide Re-Evaluation Division (PRD) can consider higher tier data. EFED will not be amending the Draft Ecological Risk Assessment for Registration Review to include additional refined analyses.

(11) Comment: ***Terrestrial Invertebrate Risk Characterization: Bee Exposure Assessment:***

a) The US EPA states that the colony feeding study endpoints are not suitable for risk assessment because of a lack of analytical confirmation that the dosing solutions were prepared correctly. Analytical confirmation is not the only source of information available to determine whether the dosing solutions were prepared correctly. This study was conducted under Good Laboratory Practices (GLP) which requires extensive and thorough documentation of all procedures conducted during the study, including during the preparation of the dosing solutions.

None of these guidance documents and publications require analytical confirmation of the dosing solutions to achieve valid scientific results. In conclusion, the colony feeding study (MRID 50271704) does provide sufficient, accurate and scientifically valid evidence of the lack of effects of mancozeb on honey bee colonies at the reported test concentrations, and the study should be considered suitable for risk assessment.

b) Because mancozeb does not exhibit systemic transport in plant fluids, the only way mancozeb residues can be found in nectar is by contact with the spray solution immediately after spraying. Mancozeb concentrations in nectar are limited by solubility to no more than between 0.67 mg/L to 16 mg/L. Correcting for the density of 50% sugar content of nectar (1.2 kg/L), the maximum concentration of mancozeb achievably dissolved in nectar is between 0.56 mg/kg to 13 mg/kg. Refinement of the Off-Field risk assessment should also take into consideration the maximum solubility of mancozeb achievable in nectar.

EPA Response:

In response to bullet (a), even when following all GLP standards human error is still a possibility. There can be errors in any step of the process and analytical verification is the best way to confirm dosing. Analytical verification is not required in accordance with OECD test guidelines, therefore this study was not deemed invalid. The study was still used, as practicable, for qualitative characterization of possible risk to honey bees.

In response to bullet (b), while there may be some evidence available that shows mancozeb is not systemic, EFED has not made a full evaluation of this information for the bee risk assessment. There were also no studies available that measured the concentration of mancozeb or its degradate residues in pollen and nectar. Refinement of an off-field risk assessment based on residue values is not typical in an EFED bee risk assessment.

III. Agricultural Aviation Association (NAAA) Comments

(1) Comment: ***Use of Tier 1 model in AgDRIFT:***

NAAA disagrees that the Tier 1 model in AgDRIFT and associated assumptions should be used to assess the risk of drift from aerial applications of mancozeb or other pesticides. NAAA provided a detailed explanation of the erroneous assumptions in the Tier 1 AgDRIFT model and proposed the use of the Tier 3 AgDRIFT model instead, in a letter to the Office of Pesticide Programs in June of 2020. The use of the Tier 1 model in AgDRIFT results in unrealistic drift estimates from aerial applications that then vitiate all of the additional modeling and assessments that use the faulty estimate.

EPA Response:
AgDRIFT is the currently approved model for evaluating potential spray drift from a pesticide application. The agency appreciates the additional suggestions provided by NAAA for revising the AgDRIFT modeling inputs and continues to work with industry to update and improve modeling methods to better reflect typical application practices. At the recent December 2020 Center of Excellence in Regulatory Science in Agriculture (CERSA) workshop, EPA, NAAA, and other stakeholders discussed these potential refinements for AgDRIFT modeling. EPA is currently reviewing these suggestions and will consider them for future risk assessment. However, modeling for a national-level assessment is first conducted using maximum application rates, limitations, and instructions listed on the mancozeb labels. In the absence of specific use directions and application restrictions implemented across all product labels, default assumptions (based on empirical data) are used.

IV. The United States Department of Agriculture (USDA) Comments

(1) Comment: *Modeled Application Rates:*

While USDA understands that it is EPA's policy to evaluate the maximum labeled application rate for each use pattern, we note that this can sometimes lead to overly conservative exposure and risk estimates. USDA requests that EPA take the typical use rates into account when characterizing the ecological risk assessment conclusions for all taxa.

EPA Response:

Typical use rates are provided by the Biological and Economic Analysis Divison (BEAD) and will be considered by the risk manager to characterize exposure and determine appropriate mitigation measures.

(2) Comment: *Foliar Dissipation Half-life:*

EPA's analysis of risk to terrestrial vertebrates relies on the default assumption of a 35-day foliar dissipation half-life for mancozeb. Because multiple applications are modeled for each use pattern, refinement of the foliar dissipation half-life would impact the modeling results. Fantke et al. (2014) reported a mean foliar dissipation half-life for mancozeb of 4.69 days (95% CI: 4.29-5.13 days).

EPA Response:

The Agency would need to access the raw data included in the Fantke et al. open literature paper to assess the applicability and validity of these data to possibly refine the mancozeb foliar dissipation half-life. At this time, such data is not in EPA's possession. Other comments suggested refinements to the default half-life (reduction to 17.6 days) however those changes would not impact the risk conclusions presented in the draft risk assessment.

V. The UPL NA Inc. and UPL Delaware, Inc. (UPL) Comments

Comments on EPA Document: "Mancozeb: Draft Ecological Risk Assessment for Registration Review (DP Barcode: 457306)"

(1) UPL Comment on EFED risk conclusion summary:

a) *UPL would like to note that the EFED preliminary ecological risk assessment is overly conservative by considering non-realistic input values based on strict, sterile water laboratory conditions. Mancozeb is highly susceptible to hydrolysis with reported DT_{50} values < 1 day (DT_{90} < 3 days). Hydrolysis is the main process for forming the major aquatic metabolite, ETU. In addition, under non-sterile aquatic conditions, ETU also rapidly degraded (DT_{50} ~ 2.3 days). Also, given the rapid soil degradation of mancozeb (soil DT_{50} < 1 day), exposure via run-off is low. Spray drift is the dominant route of entry into water bodies. As mancozeb is shown to have a short half-life in aqueous environments, exposure to aquatic organisms from the parent under natural conditions are minimal. Even under anaerobic conditions due to rapid hydrolysis, mancozeb breaks down before anaerobic conditions (in soil and/or water) develop after application.*

b) *When it comes to a rapidly degrading active such as mancozeb, maintaining continual exposure via flowthrough or semi-static laboratory study designs is overly conservative, and the toxicity endpoints derived from such laboratory studies are not reflective of the actual potential behavior of the parent molecule. This should also be considered when mitigation measures are proposed, as Tier 1 AgDrift distances are based on considering the high toxicity of mancozeb to aquatic organisms and not the rapid degradation into less toxic metabolites, especially when considering chronic exposure.*

c) *In addition, prior to reporting buffer distances from off-site spray-drift, AgDrift model does allow for higher tier (refined) EECs to be estimated. Tier III assessment should be considered, as repeatedly supported by NAAA responses for most molecules. It should also be noted that a medium to coarse droplet size for mancozeb uses is common practice and fine droplet sizes are not considered. These parameters at the least should be considered in a higher tier assessment.*

EPA Response:

In response to bullet (a), degradation in water is considered as part of the fate modeling process and does impact the EEC's reported in the risk assessment document. It is noted that all fate parameters, mentioned in UPL comment, for mancozeb and EBIS and ETU were considered in modeling.

In response to bullet (b), the methods for toxicity testing are standard and protective of all possible exposures and chemicals.

In response to bullet (c), AgDRIFT is the currently approved model for evaluating potential spray drift from a pesticide application. The agency appreciates the additional suggestions provided by NAAA for revising the AgDRIFT modeling inputs and continues to work with industry to update and improve modeling methods to better reflect typical application practices. However, modeling for a national-level assessment is first conducted using maximum application rates, limitations, and instructions listed on the mancozeb labels. In the absence of specific use directions and application restrictions implemented across all product labels, default assumptions (based on empirical data) are used.

(2) UPL Comment on EFED Terrestrial Bird and Mammal Risk Assessment

a) *Estimated Environmental Concentrations (EECs) for birds and small mammals contained in the EFED Preliminary Ecological Risk Assessment are based on the standard T-REX scenarios. EECs contained in the risk assessment are overly conservative (too high).*

   Mancozeb is known to rapidly degrade under natural environmental conditions and conducting the Tier 1 T-Rex model using default values, i.e. DT_{50} of 35 days and maximum residue values (upper-bound Kenega, mean Kenega values are more appropriate for chronic exposure), overestimates the exposure. When only considering a more appropriate DT_{50} value, the RQs are considerably lower. Consideration of a longer half-life to account for ETU should not be considered. As stated in the EFED assessment the residue of concern (ROC) is mancozeb parent only for terrestrial organisms; exposure to food items is expected to be from applied mancozeb in addition to low concentrations of ETU. Refined RQs have been calculated with consideration of the DT50 value of 17.6 days for mancozeb that also addresses the decline of ETU on vegetative feed items.

b) *Furthermore, no adverse reproductive or offspring effects were observed in the two-generation reproduction study (MRID 41365201) up to the highest dose tested (68.9/79.4 mg/kg/day in males/females, respectively). A decrease in bodyweight is unlikely to affect population growth, as seen in the laboratory study where both males and females were reported to have statistically significant lower bodyweights even during the pre-mating period. Changes in bodyweight are quite normal in mammalian species and do not reflect impaired fitness as long as the changes are within the normal range for the species concerned.*

c) *It is also noted that refined assessments were not considered in the current EFED risk assessment. As chronic risk was identified for birds. High tier modelling should be used further to refine the risk through the use of Terrestrial Investigation Model (TIM, version 3.0 beta) and the Markov Chain Next Productivity (McNest) models.*

EPA Response:

In response to bullet (a), the purpose of EFEDs ecological risk assessment is to first determine a conservative estimate of possible risk at a national level. Those risks may be further refined using additional data and/or assumptions which vary in the level of conservatism. Currently, there is insufficient data to refine the default foliar half-life for this chemical. Also, in the ROC section it states that the reason ETU is not a residue of concern for terrestrial organisms is because of modeling constrains with the current system rather than a lack of toxicity or exposure.

In response to bullet (b), changes in body weight (growth) are a widely accepted biological and apical endpoint for use in ecological risk assessment in accordance with Agency policy[6]. Effects on growth may be indicative of a wide variety of chemical mechanisms of action and are considered important for organism and population fitness. Even when considering as characterization (which was presented in the DRA) the LOAEC as the endpoint used in modeling risk, there is still the possibility for chronic risk to mammals with RQs exceeding the LOC. If PRD wants or needs additional characterization about estimated risk to inform their mitigation decisions that is up to them.

In response to bullet (c), this work has been submitted as part of another comment. Within the risk management decision-making process the Pesticide Re-Evaluation Division (PRD) can consider higher tier data. EFED will not be including additional refined analysis in the Draft Ecological Risk Assessment for Registration Review.

(3) UPL *Comment on EFED Honeybee Risk Assessment Conclusions*

a) *As for the chronic adult oral toxicity study (MRID 50271703) and colony feeding study (MRID 50271704), the studies, EFED considered these data as supplemental due to a lack of analytical verification. However, it should be stressed that the test solutions were prepared fresh every day right before administration of feed in both studies under GLP. For the colony feeding study, dose rates were prepared individually by weighing the appropriate amount of test substance and then adding sugar/water solution, with no potential error in dosing via diluting to lower test rates. It is highly uncommon that incorrect dosing would have occurred in both studies from reputable laboratories. The uncertainty in the toxicity endpoints should be minimal, and the data can be considered to support a low risk to both adult and larvae honeybees. According to EFED's assessment, even with assumed uncertainty in dosing, based on a conservative Tier 1 BeeRex estimate, the EECs in pollen and nectar correspond to up to 528 mg a.i./kg food (4.8 lbs a.i./A), and are similar to the dietary concentrations tested in the colony feeding study. If dosing were not accurate, any variation would be compensated by the conservatism of the EFED bee model.*

[6] https://www.epa.gov/risk/ecosystem-services-ecological-risk-assessment-endpoints-guidelines

b) *Exposure off-field would also be considerably less than that predicted by the Tier 1 AgDrift values presented in the EFED assessment. If deemed necessary, a higher tier off-field assessment should be considered (Tier III AgDrift) prior to setting off-field spray drift buffer zones.*

EPA Response:

In response to bullet (a), even when following all GLP standards human error is still a possibility. There can be errors in any step of the process and analytical verification is the best way to confirm dosing. While analytical verification is not required in accordance with OECD test guidelines, this study was also not deemed invalid. The study was still used as practicable for qualitative characterization of possible risk to honey bees.

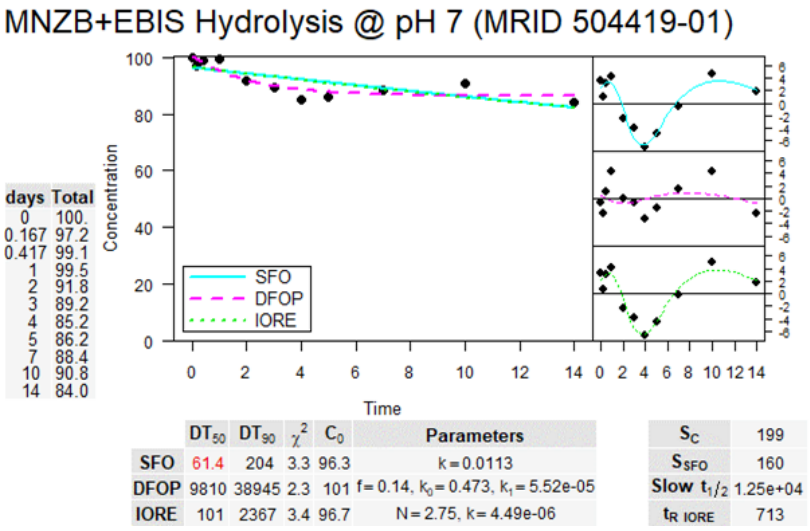
In response to bullet (b), AgDRIFT modeling inputs for a national-level assessment is first conducted using maximum application rates, limitations, and instructions listed on the mancozeb labels. If PRD needed higher tier off-field assessments before setting spray drift buffer zones they can request that.

Comments on EPA Document: "Mancozeb: Drinking Water Assessment to Support Registration Review (DP Barcode: 459932)"

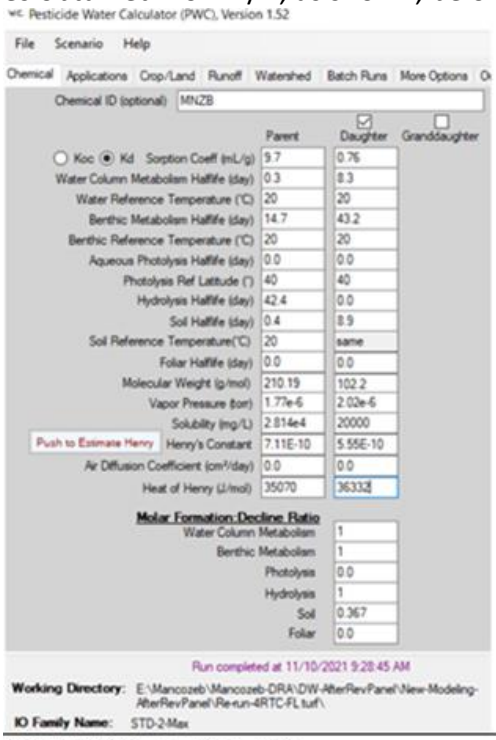
(1) Comment: *Hydrolysis half-life (t1/2) of 61.4 days for parent (mancozeb + EBIS) and aerobic soil half-life (t1/2) of 13.4 days for ETU based on formation and decline approach were used as modeling input parameters for surface water aquatic modeling and ground water modeling (Table 2, page 5). However, the actual t1/2 values should be 42.4 days (parent) and 8.9 days (ETU) as reported on page 48 and needs to be used for surface water and ground water modeling accordingly.*

EPA Response:

Entries for hydrolysis and aerobic soil in Table 2, page 5 (of the 2020 DWA) were based on half-lives obtained from kinetic modeling, see example below for mancozeb+ EBIS (61.4 d half-life):



However, in PWC modeling, which is what EPA used to determine EDWCs in the DWA, EFED used half-lives obtained from F/D, as shown, below:



Peak 1-in-10.0 = 78.3 ppb
Chronic 1-in-10.0 = 6.71 ppb
Simulation Avg = 4.73 ppb
4-d avg 1-in-10.0 = 72.7 ppb
21-d avg 1-in-10.0 = 52.4 ppb
60-d avg 1-in-10.0 = 37.5 ppb
90-d avg 1-in-10.0 = 27.1 ppb
1-d avg 1-in-10.0 = 75.9 ppb
Benthic Pore Water Peak 1-in-10.0 = 23.4 ppb
Benthic Pore Water 21-d avg 1-in-10.0 = 22.4 ppb
Benthic Conversion Factor = 1.13 -Pore water (ug/L) to (total mass, ug)/(dry sed mass, kg)
Benthic Mass Fraction in Pore Water = 0.328

Therefore, the modeled EDWCs in the DWA are accurate. The half-life values in Table 2, page 5 of the 2020 DWA are from kinetic modeling and were listed in the DWA in error. They will be corrected in future drinking water assessments.

(2) Comment: *The surface water aquatic modeling and ground water modeling for ETU were executed using the Pesticide in Water Calculator (PWC, version 1.52) based on the maximum use pattern application rate according to GAP (mancozeb turf use). However, EPA released a new version of the PWC (Version 2.001) in 2020 and approved for regulatory use. This latest version of the PWC provides additional crop schedule options, improved sediment-waterbody interactions, and the ability to use more recent weather files. The simulation using the latest version is more robust and could have a significant impact on surface water and ground water EDWCs. Therefore, the current version of PWC could be considered for the final assessments.*

EPA Response:

The approved version of PWC was 1.52 at the time of modeling.

(3) Comment: *The acute surface water EDWC (75.9 ppb) and non-cancer chronic surface water EDWC (6.71 ppb) for ETU based on modeling (Table 1, page 2) were used for dietary risk assessments although a substantially lower and more realistic EDWC of 0.1 ppb was reported based on monitoring data for ETU from a valid two-year national monitoring survey approved by EPA (Section VI, Page 9). However, the ground water EDWC (0.21 ppb) based on monitoring data (Table 1, page 2) was used in the cancer chronic dietary risk assessments. It is clarified that acute short-term concentration for ETU might have been missed during monitoring due to only two monitoring frequencies (7-day and 30-day, page 13) and thus monitoring data was not considered for acute and non-cancer chronic dietary risk assessments. However, this approach is overly conservative considering a short aerobic aquatic half-life of ETU (8.3 days used as an input parameter for modeling) and the overall detection frequency during monitoring survey was only 2% (81 detects/3,969 surface and groundwater samples, page 11). Therefore, more realistic EDWC is expected to be between the monitored concentration and modelled EDWCs for ETU and it could be considered for acute and non-cancer chronic dietary assessments accordingly*

EPA Response:

EFED relied on the 2-year monitoring data to the extent possible giving the frequency of monitoring as well as monitored concentrations for surface and ground water. EDWCs from monitoring data was used to complement the modeling for the acute and non-cancer chronic EDWCs by giving a range for expected concentrations (from monitored to modeled concentrations). In modeling, ETU half-life of 8.3 days is one of the parameters used.