TITLE

The Conservatism of EPA's Preliminary Ecological Risk Assessment for Atrazine

TEST GUIDELINE

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COMPLETION DATE

05/17/2017

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80135

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FINAL REPORT

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Date: May 17, 2017

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Gary Marshall
Chair
Triazine Network

May 17, 2017

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This report is a Review of EPA's Ecological Risk Assessment for Atrazine and is consistent with the requirements of FIFRA. As such, it is not required to comply with 40CFR Part 160.

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INTRODUCTION

The US Environmental Protection Agency (EPA) recently released a preliminary version of the ecological risk assessment (ERA) for atrazine. Our previous review of this document indicated many shortcomings including use of poor quality data, hyperconservative assumptions and inputs, and model calculation errors. These shortcomings occurred in spite of atrazine having a very rich database for fate parameters, monitoring data, and toxicity studies. Past assessments of atrazine by EPA came to very different risk conclusions for at least some of the receptors, e.g., birds. The different conclusions in past assessments were at least partly due to use of fewer hyperconservative assumptions and more scientifically defensible methods and data. Because atrazine is a critical tool for farmers, particularly those with corn, soybean and sugarcane farms, the Triazine Network requested that Intrinsik prepare comments for submission to the EPA Administrator regarding the erosion of sound science as the basis for regulating this compound. Our comments are aimed at ensuring that EPA uses the best available science in future assessments for atrazine.

This document is organized by receptor group and focuses on the taxa that were identified as being at risk in EPA's preliminary assessment for atrazine. The text in the main body of the report is brief with the details being provided in the attached appendices.

AQUATIC RECEPTORS

EPA's aquatic risk assessments for atrazine have become more conservative since its previous assessment in 2003. In 2003, EPA determined that adverse effects to aquatic plants and fish could occur at atrazine concentrations greater than 10 to 20 µg/L. In 2016, EPA lowered the effects thresholds to 5 µg/L for fish and 3.4 µg/L for aquatic plants. The sensitivity of aquatic communities to atrazine has not changed over time. However, EPA's procedures for deriving effects metrics, as well as exposure estimates, have become increasingly conservative without any supporting scientific rationale (see Appendix A for details). Some examples:

- Although the acute effects threshold for fish did not change in the preliminary risk assessment (EPA, 2016), the chronic effects threshold was reduced 13-fold. EPA (2003) selected a chronic no observed effect concentration (NOEC) of 65 µg/L from a brook trout study (Macek et al., 1976) to be the chronic effects threshold for freshwater fish. However, in the preliminary assessment, EPA (2016) selected a chronic NOEC of 5 µg a.i./L derived from a Japanese medaka study (Papoulias et al., 2014). According to EPA's own Data Evaluation Record (Bryan et al., 2014), the Papoulias et al. (2014) study was seriously flawed. A high-quality study (Schneider et al., 2015) with the same species that followed Good Laboratory Practice (unlike the Papoulias et al., 2014 study) produced a chronic NOEC of >53 µg a.i./L. The superior study by Schneider et al. should have been used to assess chronic risks to freshwater fish rather than the flawed study used in the preliminary assessment. To compound the problem further, EPA used the flawed study to also assess risks to saltwater species, even though the flawed study was conducted with a freshwater species and acceptable toxicity studies were available for saltwater species.

- Because aquatic plants are the most sensitive receptor to atrazine, a level of concern (LOC) was derived by EPA below which no effects to aquatic plant communities would be expected. In the last several years, EPA has made multiple attempts to define the LOC for aquatic plants. Except for the most recent LOC of 3.4 µg/L in the preliminary EPA (2016) assessment, the proposed LOCs have been thoroughly reviewed by EPA's own Scientific Advisory Panels (SAP, 2007, 2009, 2012). Notably, none of EPA's previously proposed LOCs have been formally accepted or endorsed. In fact, the latest SAP (2012) review strongly recommended increasing the proposed LOC of 4-7 µg/L (EPA, 2007) because many of the community-level studies were either of unacceptable quality or did not actually cause effects of ecological significance. EPA (2016) ignored the advice of the SAP (2012) and the recommendations of other reviewers (e.g., Giddings, 2012; Moore et al., 2015, 2016) by continuing to use poor quality study results to derive the lowest LOC proposed to date. A recent evaluation that was published in a peer-reviewed scientific journal resulted in an LOC of 23.6 µg/L (Moore et al., 2016).
- Despite the availability of a comprehensive water monitoring dataset for atrazine, EPA (2003, 2016) has primarily relied on models to predict atrazine concentrations. The environmental concentrations predicted by EPA's models, however, significantly overpredict measured environmental concentrations by as much as 260-fold when compared to all available monitoring data. In their earlier assessment, EPA (2003) did incorporate monitoring data into the refined exposure estimates for streams, lakes, reservoirs, and estuarine/marine environments. Why EPA (2016) reverted to a more conservative approach and primarily relied on modeling data for their preliminary assessment is perplexing. The targeted monitoring dataset available for atrazine is extensive, robust and of the highest quality and should have been the basis for the aquatic exposure assessment.

Predictably, the hyperconservatism in EPA's fish and plant assessments led to increased risk estimates in the 2016 preliminary assessment. For example, the calculated risk quotients for fish by EPA (2016) were over an order of magnitude higher than those calculated previously even though application rates for atrazine have decreased or remained constant since the earlier assessment. Similarly, aquatic plant risk estimates increased significantly, at least partly because of the LOC of 3.4 µg/L, which is 3 to 10-fold below any other LOC for aquatic plants that has been developed by EPA or recommended by various SAPs, Giddings (2012) and Moore et al. (2016).

TERRESTRIAL PLANTS

EPA's estimated risks for atrazine to terrestrial plants increased from their 2003 assessment, despite no changes to the effects threshold and decreases or no changes in assessed application rates. The increased risk estimates were due to a change in the exposure estimation methodology. In 2003, exposure was estimated as a simple fraction of applied pesticide. The preliminary ERA used a model (i.e., TerrPlant) to estimate spray drift and runoff to non-target plants. However, as with many of the Agency's models, TerrPlant includes a number of overly conservative assumptions, including assuming maximum wind speed permitted on the label,

minimum droplet size, and others (see Appendix B for details). Furthermore, the Agency continued to rely on an effects threshold from a flawed study even though new studies that followed Good Laboratory Practice were conducted recently (i.e., Martin, 2015a,b). The effects threshold used by EPA in 2003 and 2016 was from studies by Chetram (1989a,b). However, these studies followed an outdated methodology and used nearly pure atrazine rather than the end use product that is actually applied in the field. The new studies used currently available products and updated the methodology to include evaluating plant recovery. It appears that EPA was insistent on using the study that provided the lowest threshold and therefore highest possible risk rather than rely on best available data. The increased conservativism in the terrestrial plants assessment produced higher risk estimates and larger than necessary no-spray buffers to mitigate risk to non-target terrestrial plants.

MAMMALS

In their 2003 assessment, EPA concluded that "atrazine is practically non-toxic to slightly toxic to birds and mammals". Even though the effects thresholds remained the same in the 2016 preliminary assessment, EPA concluded that atrazine posed a chronic risk to mammals. This chronic risk conclusion is solely due to a change in the method by which EPA estimates exposure. In the preliminary ERA, EPA (2016) used a modeling tool, T-REX. However, T-REX is overly conservative and assumes, for example, that: 100% of an organism's daily diet over a long duration is from a crop recently treated with atrazine, concentrations on all food items consumed by mammals are upper bound values, and atrazine has an unrealistically high persistence following application (see Appendix C for additional details). Given the relative non-toxicity of atrazine to mammals, it is doubtful that any pesticide would pass EPA's current assessment protocol for mammals.

BIRDS

When EPA conducted its risk assessment for birds in 2003, they concluded that "atrazine is practically non-toxic to slightly toxic to birds" and that "there is negligible potential for acute risk to birds". Although some chronic risks were identified, they were fairly minor. These conclusions were reached despite using a highly conservative screening-level risk model for birds (i.e., the Terrestrial Fate Residue Model) that was purposefully designed to overestimate acute and chronic risks. Conversely, in the 2016 preliminary assessment, EPA concluded that there was acute risk for plant-eating, insect-eating and omnivorous birds for nearly all use patterns. Chronic risks were also higher than predicted in the 2003 assessment. The screening-level risk model used in 2016 was the Terrestrial Residue Exposure model (T-REX, version 1.5.2). The 2003 and 2016 screening-level risk models for birds are conceptually similar. Unlike in 2003, EPA went further with their 2016 avian assessment, and used two probabilistic models, TIM and MCnest, to better characterize acute and chronic risks of atrazine to birds. The models estimated significant mortality for many species and near total reproductive failure for small and medium omnivorous and insectivorous bird species (e.g., American robin, chipping sparrow, common yellowthroat, killdeer, and vesper sparrow) that forage in corn fields treated with

atrazine. Even with application rates well below current typical rates or the rates assessed in 2003, near total reproductive failure was predicted.

So how is it that EPA reached such radically different conclusions with regard to acute and chronic risk of atrazine to birds in 2003 and 2016? The answer is not because of new studies showing increased toxicity of atrazine to birds or new fate studies indicating higher levels of atrazine on bird foods than had been predicted previously. The answer is due to EPA's use of increasingly conservative assumptions in the 2016 assessment compared to the 2003 assessment (see Appendix C for further details). These conservative assumptions were not based on sound science. Some examples:

- In its 2016 assessment, EPA used a default 35-day foliar dissipation half-life, despite acknowledging the availability of field studies showing that the half-life ranges from a few to 17 days. Longer half-lives lead to higher estimates of chronic exposure and risk.
- The highest acute and chronic exposures predicted by EPA in 2016 were for very small birds (20 grams) that only consume short grass in areas recently treated with atrazine. No such bird exists, however, because such a small bird cannot digest grass sufficiently and rapidly enough to provide the energy required to sustain itself.
- Using the same mallard reproduction test as in the 2003 assessment, EPA reduced the chronic effects threshold >3-fold. The rationale for the reduction, however, was based on a flawed statistical analysis.
- The 2016 probabilistic assessment considered dermal exposure. This route of exposure was estimated to contribute 80% of the overall dose for birds. However, dermal exposure dominating over oral exposure does not make logical sense. Birds have feathers that intercept and significantly decrease dermal exposure. Also, birds typically evacuate the area during application and therefore are unlikely to come into direct contact with spray. Following application, atrazine becomes rainfast within 1-2 hours and thus is far less available for dermal exposure via contact with the foliage. To further compound the issue, EPA vastly overestimated dermal toxicity of atrazine by extrapolating from data for insecticides that are far more toxic than atrazine.
- In the 2016 assessment, EPA used a lower acute effects metric. The change was based on a re-analysis of the data, a change supported by the Triazine Network's own re-analysis of the data. However, EPA mistakenly retained the slope of the dose-response curve from the old analysis rather than use the slope from the re-analysis. This error led to a significant overestimate of acute risk to birds.
- The basis for EPA's estimate of the rate at which birds metabolize and detoxify atrazine was not adequately described in the 2016 assessment. Our review of the available data, however, indicated a much more rapid rate of metabolism. As expected, using the more scientifically justified rate of metabolism led to a considerable reduction in the predicted effects of atrazine on birds.
- The cumulative error of many incorrect inputs results in highly conservative and inaccurate risk estimates for birds. Selection of correct model inputs results in negligible risk estimates for birds, as would be expected for birds exposed to an herbicide that has no record of having caused bird kills in over 50 years of use.

When real-world data are considered, it is obvious that the 2016 risk estimates were grossly overstated. Despite atrazine having been one of the most widely used herbicides in the United States since being registered in 1959, the EPA's own incident databases indicate a complete lack of bird incidents in the last 10 years. Further, according to the US Geological Survey's Breeding Bird Survey, many of the bird species predicted to be at significant risk from atrazine exposure have experienced strong and sustained population increases in areas where atrazine has been most intensively used over the last 50 years, while experiencing decreases in areas where atrazine use has been lower.

CONCLUSIONS

The preliminary risk assessment recently released by EPA (2016) for atrazine was overly conservative, relied on poor quality data, and had a number of errors. A number of issues are highlighted in this report and include the following:

- EPA's aquatic and terrestrial exposure modeling relied on highly conservative assumptions that are not representative of atrazine use areas and the organisms that live there.
- The best available effects data were not employed for fish, aquatic and terrestrial plants, and wildlife. Instead, EPA often relied on poorer quality data simply because they produced more conservative effects thresholds.
- Numerous issues were identified in EPA's refined avian assessment. When best available data are used as inputs to the exposure model, avian risks are negligible.
- The calculation of a level of concern for aquatic plants relied on poor quality data that have previously been rejected by multiple sources (SAP, 2009; 2012; Giddings, 2012; Moore et al., 2015; 2016).

Atrazine has an incredibly rich database of information with regard to exposure and effects to aquatic and terrestrial organisms. Numerous Scientific Advisory Panels have also given thoughtful recommendations and advice to the EPA that, if accepted, would have led to a far less conservatively biased and more scientifically defensible assessment. EPA, however, ignored this advice and the availability of much high quality scientific information in favor of making decisions that significantly overestimated ecological risk.

There are several obvious consequences to overestimating risks, particularly in a high profile case such as atrazine:

Loss of regulatory credibility

Atrazine has been widely used for decades in the United States and undergone assessment and reregistration by the EPA on several occasions. What must the public think about an agency charged with protecting the environment suddenly finding that their assessment and registration process failed, on a grand scale, to protect, for example, bird communities in the Midwest? Even though the atrazine assessment is in preliminary form and may ultimately be revised, the damage to the EPA's credibility with the public will be difficult to reverse.

Loss of important tools for agriculture

According to the National Corn Growers Association, farming without atrazine would cost corn farmers US$30 to US $59 per acre. Thus, its continued use saves US farmers up to US$3.3 billion per year and consumers up to US$4.8 billion per year. Atrazine is also an important tool for weed resistance management.

There are, of course, many other consequences associated with overestimating the risks of atrazine. Clearly, time, effort, and resources must be invested in developing a more scientifically defensible ecological risk assessment for atrazine.

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Appendix A
Risk Assessment for Aquatic Receptors

A.1 Chronic Effects Threshold for Freshwater Fish

EPA (2016) selected a chronic exposure study using Japanese medaka (*Oryzias latipes*) (Papoulias et al., 2014) as the basis of their chronic effects metrics for both freshwater and estuarine/marine fish. Papoulias et al. (2014) exposed breeding groups of one male and four females to atrazine in a static renewal system for up to 38 days. Nominal test concentrations were 0.5, 5.0, and 50 µg/L. The authors found reduced egg production at all treatment levels.

The study (Papoulias et al., 2014) was flawed, as EPA noted in its own Data Evaluation Record (DER) (Bryan et al., 2014). The study did not follow a standard guideline, had high intra-treatment variability, particularly in the solvent control treatment, and did not demonstrate a clear concentration-response relationship (Bryan et al., 2014). EPA further highlighted other limitations of the study, including lack of a true negative control treatment, a high female to male ratio (4:1 versus 1:1), no results reported for time zero sampling, low fecundity in the control treatment (9.7 eggs/female/day), and high mortality in the solvent control. The study authors found significant effects to egg production and reproduction at all treatment levels (NOEC <0.5 µg/L), but EPA (2016; Bryan et al., 2014) re-evaluated the study data and determined a NOEC of 5 µg/L and a LOEC of 50 µg/L. In fact, all differences in egg production were within the variability of the dataset, high variability was noted throughout the test, and only weak statistical evidence of an atrazine effect was observed at 50 µg/L (Bryan et al., 2014).

Because of the many flaws in the Papoulias et al. (2014) study, Syngenta sponsored a Good Laboratory Practice (GLP) study on Japanese medaka that followed standard testing protocols (GLP; OCSPP Guideline 890.1350; OECD 229) to provide a higher quality study for use in future risk assessments (Schneider et al., 2015 [MRID 49694001]).

Schneider et al. (2015) exposed Japanese medaka to atrazine under flow-through conditions for 21 days. Nominal exposure concentrations were 0, 0.49, 4.9, and 49 µg a.i./L, which corresponded to mean measured concentrations of <0.125, 0.59, 5.4, and 53 µg a.i./L, respectively. Schneider et al. (2015) found no significant effects on fecundity or fertility at any treatment level. Control fecundity was 40.9 eggs/female/day, compared to 9.7 eggs/female/day in Papoulias et al. (2014). Mean control fertility in Papoulias et al. (2014) was 62%, while mean control fertility in Schneider et al. (2015) was 91.7%. Only the Schneider et al. (2015) study meets the OECD guidelines, which require ≥80% fertility.

Schneider et al. (2015) made several improvements to the study design used by Papoulias et al. (2014) including use of a flow-through exposure system, achieving much higher fecundity in controls, no reliance on solvent, and alignment with recommended guidelines. Therefore, Schneider et al. (2015) offers significantly higher data quality than the Papoulias et al. (2014) study used upon by EPA (2016) in their ERA for atrazine. Schneider et al. (2015) were not able to reproduce the results of Papoulias et al. (2014). In fact, the higher quality study found no treatment-related effects at the test concentrations previously used by Papoulias et al. (2014), further decreasing the scientific credibility of the effects threshold used in the ERA.

EPA also evaluated Schneider et al. (2015) in a DER (Marton et al., 2015). The reviewers determined that the study was scientifically sound and the methods used were generally consistent with OCSPP guideline 890.1350. Marton et al. (2015) agreed with the study authors

that no significant treatment-related effects were observed at any test concentration. Therefore, we recommend that EPA re-consider the effects threshold used in their preliminary ERA with the goal of relying on best available data, rather than lower quality data simply because the latter produces a lower threshold.

A.2 Chronic Effects Threshold for Estuarine/Marine Fish

EPA (2016) used the flawed Japanese medaka study summarized above (Papoulias et al., 2014) as a surrogate effects metric for chronic effects to estuarine/marine fish. However, EPA (2016) provided no support or rationale for their choice nor did they provide evidence indicating that freshwater and estuarine/marine fish have similar sensitivities to atrazine. Further, EPA (2016) ignored a chronic marine fish study that is available for sheepshead minnow (Cafarella, 2005 [MRID 46648203]), an estuarine fish species. In their previous 2003 assessment, toxicity data for estuarine/marine fish were used.

Under GLP conditions, Cafarella (2005) exposed fertilized sheepshead minnow eggs from 26-hours post-fertilization to 28 days after hatch to concentrations of atrazine (FL-881692; 97.1% purity) ranging from 200 to 3200 µg /L. Mean measured concentrations were 150, 300, 570, 1100, and 2200 µg /L. Larval length and wet weight were the most sensitive endpoints, resulting in a no observed effects concentration or NOEC of 1100 a.i./L. This effects threshold is over 200 times higher than the freshwater effects threshold from the flawed Japanese medaka study (Papoulias et al., 2014) used by EPA in their preliminary assessment.

EPA previously scored the Cafarella (2005) study as supplemental because it did not fulfill guideline requirements (Volz, 2006 [MRID 46952604]). The flaws highlighted by EPA included: the study only maintained two replicate aquaria, did not assess time to hatch, and the study duration was 28 days post-hatch instead of the recommended 32 days. Syngenta subsequently amended the reported and provided support for re-scoring of the study (Volz, 2006). The issues are addressed below:

- Description of test substance: Provided to EPA in amended report.
- Replication: Current OPPTS Guidelines (850.1400) recommend at least two replicates, with 60 eggs total. Cafarella (2005) had 40 eggs per replicate, and thus 80 eggs per treatment. The guideline requirements were met.
- Duration: OPPTS Guideline 850.1400 clearly states that the study should last 28 days post-hatch for sheepshead minnow. This duration was used in the original study (Cafarella, 2005).
- Reporting of dilution water analysis: Provided to EPA in amended report.
- pH range: According to OPPTS Guideline 850.1400, a pH range of >7.5 to <8.5 is appropriate for marine testing. This is consistent with the pH range of 7.8 to 8.2 measured by Cafarella (2005).
- Time to hatch: Although treatment effects on time to hatch were not directly evaluated to avoid injuring newly hatched fry, percent hatch was determined on Day 5. On Day 5, percent hatch among treatments and controls was not significantly different, indicating that atrazine did not affect hatch.

Based on data provided in the amended report and consistencies between the original study methods and OPPTS guideline 850.1400, this study is appropriate for use in a risk assessment and should have been used by EPA in their atrazine assessment for estuarine and marine fish. For the reasons described above, EPA (2016) had no scientific justification for relying on a poorly conducted freshwater fish study as the basis for the chronic effects threshold for estuarine and marine fish, particularly given the availability of a well-conducted chronic study on sheepshead minnow, an estuarine species.

A.3 Effects Threshold for Aquatic Plants

As an herbicide, plants are expected to be more sensitive to atrazine than other receptors. Therefore, to ensure that atrazine concentrations in watersheds will not cause ecologically-significant effects to aquatic plant communities, EPA developed a community-level level of concern (LOC). The LOC was compared to exposure data to determine which watersheds have atrazine concentrations that could cause adverse effects to aquatic plants.

Over the last several years, EPA has made multiple attempts to define the LOC for community-level effects of atrazine to aquatic plants. These LOCs have become increasingly conservative over time. Except for the most recent LOC of 3.4 µg/L in the preliminary EPA (2016) assessment, the proposed LOCs have been thoroughly reviewed by EPA's own Scientific Advisory Panels (SAP, 2007, 2009, 2012). Notably, none of EPA's proposed LOCs have been formally accepted or endorsed. In fact, the latest SAP (2012) review strongly recommended increasing the proposed LOC of 4-7 µg/L (EPA, 2007) because many of the higher tier mesocosm studies purportedly showing effects at low concentrations were either of unacceptable quality or did not actually cause effects of ecological significance. However, EPA (2016) ignored the advice of the SAP (2012) and the recommendations of other reviewers (e.g., Giddings, 2012; Moore et al., 2015, 2016) by continuing to use poor quality mesocosm study results to derive the lowest LOC that has been proposed to date.

The SAP (2012) recommended evaluating mesocosm studies using a standard set of scoring criteria. The SAP (2009, 2012) also recommended that EPA re-evaluate and re-score all cosm studies where effects were observed at concentrations less than 30 µg/L because of weaknesses in study design and data interpretation (see also Giddings, 2012). The SAP (2012) identified a number of studies that were incorrectly scored by EPA as having effects when in fact, no effects were observed during the studies or the studies were clearly of poor quality. Further, the SAP (2012) requested that the LOC be recalculated once the studies were re-scored.

The results of Giddings (2012), two SAPs (2009, 2012) and Moore et al. (2015, 2016) demonstrate that no statistically and ecologically significant effects have occurred at atrazine concentrations below 30 µg/L. Moore et al. (2015, 2016) also evaluated new mesocosm studies published since the SAP (2012) review (Baxter et al., 2013; Choung et al., 2013; Halstead et al., 2014; Knauer and Hommen, 2012; Murdock and Wetzel, 2012). In these studies, no effects were observed at concentrations less than 30 µg/L. Therefore, EPA's 60-day LOC of 3.4 µg/L is almost an order of magnitude lower than the lowest reliable effects concentrations observed in mesocosm studies, and is overly conservative.

The mode of action of atrazine is reversible upon removal of atrazine exposure at the target site of both terrestrial and aquatic plants (Brain et al., 2012a,b; Brockway et al., 1984; Hughes et al., 1988; Jensen et al., 1977; Jones et al., 1986; Juttner et al., 1995; Klaine et al., 1996; Mohammad et al., 2008, 2010; Moorhead and Kosinski, 1986; Shimabukuro et al., 1970; Stay et al., 1985, 1989; Vallotton et al., 2008). Monitoring data from the Atrazine Ecological Exposure Monitoring Program (AEEMP) have shown that the median duration of concentration peaks greater than 15 µg/L is 2 days (Brain, 2012). Atrazine is likely to enter natural systems as pulses during runoff events. Independent of degradation, water dynamics, flow and dilution would disperse the atrazine away from the point of input and decrease the concentration quite rapidly, particularly in larger flowing water bodies. Decreasing concentration levels would immediately allow for recovery of aquatic communities (Brain, 2012). Therefore, the increasingly conservative LOCs proposed by EPA have been overly protective of aquatic communities and unnecessarily low.

A.4 Aquatic Exposure Assessment

Despite the availability of the comprehensive and scientifically robust AEEMP dataset for atrazine (i.e., 288 site-years of daily or nearly daily data from 70 most vulnerable watersheds between 2004 and 2015), EPA (2016) primarily relied on a highly conservative model, the Surface Water Concentration Calculator (SWCC) to predict atrazine concentrations for a variety of regions and use patterns. The model scenarios were intended to be conservative and represent the 90th percentile most vulnerable sites for first-order streams and static water bodies adjacent to atrazine use areas.

Compared to available monitoring data, SWCC over-predicted peak daily and 60-day average concentrations by as much as 260-fold.

EPA's SWCC and other screening-level models should not be used to make regulatory decisions for atrazine. Unlike most pesticides, a scientifically robust targeted monitoring dataset exists that can be used to estimate atrazine exposure to aquatic organisms. To evaluate specific use patterns, EPA should consider using more refined watershed models such as the Soil Water Assessment Tool (SWAT).

EPA's standard screening-level models are not designed to identify the specific geographical locations where atrazine might truly pose a risk to aquatic organisms, a seemingly more useful approach for decision making. Refined watershed level modeling is a superior approach for such assessments because it provides exposure predictions at a fine geographical resolution with the ability to simultaneously simulate varying site-specific weather, soil, environmental, and cropping conditions within a watershed. Watershed modeling also simulates variation in pesticide application timing, and proximity of treated fields to surface water bodies and riparian areas. Moreover, watershed level modeling simulates flowing and non-flowing water bodies as well as site-specific hydrologic conditions, water body depths and water body geometries. Examples of available watershed models that could have been used in the atrazine risk assessment include the SWAT, the Agricultural Policy EXtension (APEX) model, the Hydrologic Simulation Program-Fortran (HSPF) model and the Pesticide Root Zone Model – RIVerine

Water Quality (PRZM-RIVWQ) model. All of these models, particularly the SWAT model, have undergone validation testing and have been shown to perform well.

Appendix B
Risk Assessment for Terrestrial Plants

For terrestrial plants, EPA (2016) chose effects endpoints from Chetram (1989a,b). Both the seedling emergence and vegetative vigor studies were performed according to GLP and evaluated the effects of atrazine on ten crops: soybean, lettuce, carrot, tomato, cucumber, cabbage, oat, ryegrass, corn, and onion. The Chetram (1989a,b) studies are outdated and did not evaluate recovery. A recovery phase is an important study design component for herbicides such as atrazine that have a reversible mode of action following cessation of exposure. In fact, European Food Safety Authority (EFSA, 2012) guidance recommends that the potential for ecological recovery be integrated into risk assessments for terrestrial plants.

Recently, new seedling emergence (Martin, 2015a [MRID 49639102]) and vegetative vigor (Martin, 2015b [MRID 49639101]) studies were performed using a current product (Atrazine SC; 43.0% a.i.). The new studies followed GLP, OCSPP Guideline 850.4100 and OECD 208. The Martin (2015a,b) studies applied a typical end-use product, which is required for OCSPP 850.4100 guidelines. Conversely, the Chetram (1989a,b) studies applied technical atrazine, which is not what terrestrial plants would be exposed to from spray drift in the field.

The Martin (2015a,b) studies included a recovery phase to determine the long-term effects of atrazine application on terrestrial plants. In the seedling emergence study, Martin (2015a) observed recovery in cabbage and tomato shoot lengths and dry weights. Other species either exhibited no recovery or recovery was not statistically significant.

In the vegetative vigor study, Martin (2015b) applied Atrazine SC to crops. Observations were made at 21 and 42 days after application to determine effects and the potential for recovery. Recovery was observed for all species, except for corn (which experienced no adverse effects) and shoot dry weight for oat.

When evaluating the effects of an herbicide on the terrestrial environment, the potential for recovery must be considered. Agro-ecosystems in dynamic environments are likely to recover from disturbances (e.g., pesticide applications), especially disturbances that mimic historical events (e.g., previous pesticide applications; Denslow, 1985; Rapport et al., 1985; Moore, 1998).

Recent studies with terrestrial plants suggest that tested species generally recover following single and repeated exposures to atrazine at environmentally relevant application rates. Dalton and Boutin (2010) applied atrazine to microcosms and single species to determine the potential for effects and recovery. Nine terrestrial and seven wetland plant species (1 monocot and 15 dicots) found in Eastern Ontario and Western Quebec were evaluated. Short-term experiments were 28 days and long-term experiments spanned 60 and 70 days for terrestrial and wetland microcosms, respectively. AAtrex® 480 (Syngenta Crop Protection; 470.4 g a.i./L) was applied at doses selected to achieve 20 to 80% effect in target species. Some recovery was observed in the long-term microcosms, and effects levels were higher for total microcosm biomass in longer-term microcosms than in the 28-day greenhouse microcosms.

There is no scientific justification for EPA (2016) excluding two high quality terrestrial plant studies that follow standard guidelines and use a current product (i.e., Martin et al., 2015a,b). In

addition, it is critical that recovery be considered for herbicides such as atrazine. Herbicides are developed to eradicate unwanted plants. Therefore, it is understandable that spray drift and runoff to non-target areas could cause negative effects to non-target plants. However, if recovery is possible, it could mitigate the initial effects of atrazine and show that non-target plants are able to tolerate higher exposures than assumed by EPA using shorter toxicity tests.

For terrestrial plants, TerrPlant was used to model both ground spray and aerial applications of atrazine. The limitations, assumptions and sources of uncertainty in the TerrPlant model are highlighted below (see Trask et al., 2010a,b for more details).

- *The spray drift component of TerrPlant only considers the application method and does not include additional factors such as wind speed, droplet size and height of pesticide release that may affect the quantity of pesticide moving off the field as spray drift. The no spray buffer distance is based on the application rate observed to cause no effect to the most sensitive non-target terrestrial plant species.*

- *TerrPlant conservatively assumes that runoff occurs at the time of application, an unlikely event given that farmers generally avoid applying pesticides on rainy days or when rain is in the immediate forecast.*

- *Both runoff and spray drift are assumed to be distributed uniformly throughout the non-target area. In reality, there is typically a decrease in the quantities of runoff and spray drift reaching areas of increasing distance from the application area.*

- *TerrPlant assumes that runoff and spray drift reach the non-target area at the same time and that non-target plants exposed to the pesticide residues are in the sensitive, early emergent life stages. Both of these assumptions are conservative.*

- *The fraction of pesticide in runoff is based upon estimates of pesticide solubility. Other environmental fate parameters that would likely affect the fraction of pesticide in runoff, such as K_d of the pesticide, are not considered.*

- *TerrPlant assumes that the method of exposure in standard plant toxicity tests (i.e., an overhead spray that provides even coverage of the foliage or soil surface) is analogous to what off-field non-target plants experience in the field. In reality, off-field plants experience spray drift as a fraction of the applied rate moving primarily laterally away from the application area. When surrounding vegetation is present, there may be considerable interception of drift very close to the treated field such that much reduced drift amounts reach plants downwind of the treated area. A recent field study conducted by Brain et al. (2017) with the herbicide mesotrione demonstrated that simulations of real-world exposure lead to much reduced estimates of the distance to no effects from treated fields. This and other similar studies indicate the conservativeness of EPA's assessment approach for terrestrial plants.*

Appendix C
Risk Assessments for Birds and Mammals

C.1 Effects Thresholds for Birds and Mammals

EPA (2016) selected an acute LD50 of 783 mg a.i./kg bw and a slope of 2.263 to estimate acute risks to birds. Although the original study reported an oral LD50 of 940 mg a.i./kg bw with a corresponding slope of 2.263 (Fink, 1976 [MRID 00024721]), the LD50 used by EPA (2016) was recalculated from raw data provided in the original study. EPA (2016) re-analyzed the raw data using probit analysis, resulting in an LD50 of 783 mg a.i./kg bw and a probit slope of 3.836. However, when generating effects metrics for the preliminary ERA, EPA (2016) paired the recalculated LD50 with the probit slope reported in the original study. This is incorrect. The correct LD50 and slope should be 783 mg a.i./kg bw and 3.836, respectively.

To estimate chronic risks to birds, EPA (2016) selected a NOEC of <75 mg a.i./kg diet for hatchling weight and LOEC of 225 mg a.i./kg diet for egg production and food consumption (Pedersen and DuCharme, 1992 [MRID 42547101]). A number of issues have been identified with the use of these endpoints, and include the following:

- When analyzing the raw data, the dead female in the 225 mg a.i./kg diet group should have been excluded from analyses for reproduction, so as not to skew the results.
- Data for egg production were analyzed using the William's Multiple Comparison Test, which is only acceptable for continuous data (Piegorsch and Bailer, 1997). It would have been more appropriate to use the Dunnett's test (Zar, 2010). Use of the Dunnett's test would have resulted in a NOEC of 225 mg a.i./kg diet and LOEC of 625 mg a.i./kg diet. When calculated with the appropriate statistical analyses, the endpoints are at least three-fold higher.
- The NOEC selected by EPA (2016) for hatchling weight is likely the result of inherent variability in hatchling weights and not ecologically significant. In fact, the original study authors (Pedersen and DuCharme, 1992 [MRID 42547101]) noted that the lower hatchling weight values observed on day 1 were likely attributable to normal biological variation not atrazine exposure. Statistical analyses showed large variations among birds within treatments, including within controls. Therefore, the statistical significance identified by EPA (2016) is likely trivial from an ecological standpoint and a more appropriate endpoint showing clear a concentration-response relationship should be selected.
- Estimates of food consumption were calculated incorrectly by EPA (2016). Food consumption depends on a number of factors, particularly body weight. Therefore, food consumption is generally normalized to body weight. However, not only did EPA (2016) fail to normalize the data, but they also included data points for dead birds and capped the food limit at 4600 g per cage per week for reasons unstated. This led to inaccurate food consumption calculations and artificial censoring of the data. If the raw data are recalculated to normalize for body weight and exclude dead individuals, the NOEL is ≥675 mg a.i./kg diet.

For mammals, EPA (2016) selected a chronic NOEL of 3.7 mg a.i./kg bw/d to estimate long-term effects. EPA (2016) stated that their endpoint was calculated from a NOEC of 50 mg a.i./kg diet reported by Mainiero et al. (1987 [MRID 40431303]). However, the selection of the chronic

NOEL was not discussed anywhere in the assessment and we could not replicate the calculations, despite access to the raw data. Therefore, the accuracy of the NOEL is unknown.

C.2 Exposure and Risk Assessments for Birds and Mammals

EPA (2016) used T-REX version 1.5.2 in their screening-level assessment to estimate risks to birds and mammals potentially exposed to atrazine. However, T-REX relies on a number of highly conservative assumptions to estimate risk, including the following:

- One concentration normalized to application rate (i.e., residue unit dose) is used for all arthropods, despite varying residues based on location and behavior of the arthropods. For example, flying insects are likely to have much lower residues than crop-dwelling insects. For realistic dietary exposure estimates, residues should be quantified for different invertebrate groups using available pesticide data.
- The model assumes upper bound or maximum concentrations in food items for the entire duration of exposure immediately after application.
- The model assumes that wildlife obtain 100% of their daily diet from treated locations immediately after application, whereas in reality most species forage on and off the field and will vacate the area during application, only returning after the disturbance has ceased.
- The model does not allow for analysis of mixed diets and instead considers only homogeneous diets, several of which are implausible (e.g., small birds only consuming small or long grass or broadleaf foliage).
- Food ingestion rate is estimated in T-REX with allometric equations derived from Nagy (1987). However, more up-to-date equations are currently available (e.g., Nagy et al., 1999). Further, the calculations should be based on field metabolic rates, gross energies of dietary items, and assimilation efficiencies of the dietary items consumed. The latter approach accounts for the differing amounts of energy available from different food items.

In its assessment, EPA (2016) used a default 35-day foliar dissipation half-life for atrazine, despite acknowledging appropriate dissipation studies for atrazine. These studies reported a maximum observed half-life of 17 days. EPA (2012) guidance directs risk assessors to estimate a 90% upper confidence limit on a mean half-life when three or more half-lives are available. EPA (2016) failed to follow their own guidance, citing degradates of atrazine as the primary reason. However, no data were presented by EPA (2016) that support a longer half-life for atrazine or that describe the nature of residues on foliage. Further, a field study investigating atrazine residues on grain sorghum supports foliar dissipation half-lives between four and five days for "equivalently toxic" residues (Selman, 1995).

A refined risk assessment for birds was conducted using EPA's TIM and MCnest models for atrazine. However, there are numerous issues with their use in the preliminary assessment. Many of the input values chosen by EPA (2016) did not follow their own guidance or were not appropriately determined from studies and the models incorporated a number of overly

conservative assumptions that are inappropriate for a refined assessment. Some of the issues are described below and further reviewed by Olson et al. (2016):

The Assumptions in the ERA were Not Supported by Best Available Data

- EPA used a dermal effects ratio for birds that relied on data for organophosphates and carbamates, the applicability of which to atrazine are unknown. As a result of the effects ratio, 80% of the predicted exposure was contributed by dermal contact. However, birds have feathers that will intercept and significantly decrease exposure, most birds will leave a treated area during application, and atrazine becomes rainfast within one to two hours. Therefore, contact exposure is likely to be much lower.
- A dermal effects ratio for atrazine and related chemicals (i.e., triazines) is much more applicable. For example, an effects ratio produced from data for triazine compounds reduces the estimated mortality of vesper sparrows by two thirds.
- EPA did not incorporate the vast amount of field data showing the fraction of time birds spend on treated fields. Fitting distributions to the available data, rather than using worst case scenarios, is a more applicable approach for estimating the potential for exposure.
- EPA assumed a default foliar half-life of 35 days, despite a number of field studies demonstrating a half-life of 17 days or less for atrazine. Use of the default half-life was not supported and did not follow EPA's own guidance.

The ERA Contained Significant Errors that Impacted Risk Estimates

- To estimate acute risks to birds, EPA used an LD50 and slope that were calculated using different methods. When the LD50 was paired with the appropriate slope, mortality estimates were reduced by almost 50%.
- To estimate chronic risks to birds, EPA made several errors in the selection and use of statistical analyzes. When the correct statistics are used, the NOEC increases from <75 mg a.i./kg-diet to 225 mg a.i./kg-diet. This has a significant impact on chronic risk estimates.

The ERA was Hyper-Conservative

- EPA selected an arbitrary hourly fraction of pesticide retained rather than calculating one from available data. The calculated value is lower, which decreases the potential for toxicity over long-term or multiple exposures.
- Instead of using average exposure values over the duration required to elicit reproductive effects in birds, EPA used one-day peak exposure values. This greatly increased the exposure estimates.
- EPA assumed complete nest failure when exposure exceeded the no observed effect concentration (NOEC), despite studies showing only a 24% reduction in clutch size at the LOEC and modeling showing no impacts on reproductive success when the clutch size is lowered by 22%.

The issues summarized above led to significant overestimates of acute and chronic risks for birds and mammals potentially exposed to atrazine. Using the vesper sparrow as an example, EPA's conservative assumptions predicted 21.8% mortality in treated corn fields. However, this

is not supported by 50 years of incident data or field studies. When best available data are applied, negligible risks are predicted for birds and mammals as described in Olson et al. (2016).

Finally, no other lines of evidence were discussed by EPA (2016) to validate their conclusions. Some additional information should have included:

- The lack of incident reports for birds and mammals associated with atrazine exposure despite many decades of widespread use.
- The results of breeding bird surveys that indicate that many bird species that forage in corn have increased in abundance in areas where atrazine is intensively used.
- Potential avoidance, as is often observed with other pesticides at high doses.
- The implications of their assessment being based on sprayed vegetation rather than sprayed soil, which is the predominant timing of application for atrazine in corn.