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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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SUBJECT: EFED Review of Comments from Syngenta and its Contractors about the EPA Revised Environmental Risk Assessment for Atrazine

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The Environmental Fate and Effects Division (EFED) has reviewed the 60-day response document from Syngenta Crop Protection, Inc. titled "Syngenta's Comments in Response to the Notice of Availability of Environmental Fate and Effects Assessment on Atrazine to Re-registration Eligibility Decision [OPP-34237A]. In their response, the registrant identified several dominant themes which they believe have the overall effect of overstating the risk picture for atrazine. The major themes delineated in the Executive Summary of the document are addressed below. In addition, many of Syngenta's comments referred to the assessment performed by the Atrazine Ecological Risk Assessment Panel, i.e., Giddings et al 2000, "Aquatic Ecological Risk Assessment of Atrazine--A Tiered Probabilistic Approach,"and submitted to EPA by Syngenta as their probabilistic ecological risk assessment. The Agency has also received similar comments from the panel of authors of the above study in a document titled "Comments on 'Registration Eligibility Science Chapter for Atrazine, Environmental Fate And Effects Chapter." EFED has thoroughly reviewed these documents and made extensive comments on specific areas, such as the choice of technical studies included for the assessment, the validation/status of the exposure models employed, problem formulation and scope of the study, and the level or "tier" of assessment actually performed, especially in light of refined risk assessment guidelines under development by EFED. OPP has met with Syngenta and its panel of scientists to discuss these concerns, and the EFED document detailing them is attached. Therefore, this response to comments will address both general and specific statements from Syngenta and its panel of authors, and will also refer to EFED's review of the Syngenta risk assessment where noted.

Syngenta Comment

"Risk Assessment Methods Need Refinement

...The EPA has provided lower Tier I/II assessments of the ecological risk of atrazine (which) rely primarily on the extreme, worst case toxicity data available, maximum exposure values and assumptions on indirect effects on wildlife...The advanced risk assessment (Giddings et al., 2000), submitted to the EPA in January, 2001 and again with this submission, makes full use of the available information for atrazine and applies assessment methods consistent with the opinions of various scientific and regulatory bodies."

EFED Response

The EPA atrazine Environmental Risk Assessment employed probabilistic methodolgy in addition to the screening-level assessment techniques and standardized methodologies for assessing risk that EFED utilizes for all chemicals subject to FIFRA reregistration procedures. The basic methodology used by EFED was reviewed by the FIFRA Science Advisory Panel in 1996 and was determined to be adequate for identifying chemicals of concern. It is clear from EFED's deterministic (risk quotient) and the registrant's refined (probabilistic) risk assessments, in addition to EFED's Risk Characterization, which evaluated risk in aquatic environments in response to distributions of atrazine concentrations likely to be present, that both direct and indirect effects on nontarget animals are likely. EFED disagrees with the registrant, however, on the likely extent and significance of these effects on diversity and stability of natural ecosystems. More specific comments are provided below.

Syngenta Comment

"Risk Management Implications Should be Considered Within the Revised Risk Assessment

...The RED assessment does not consider numerous refinements in the assessment based on the distributions of important variables...the scientific question of effects of multiple stressors is a relative new and emerging area which merits further attention...Related directly to risk management decisions should be the potential for system recovery as has been recognized by the EPA...Finally, risk assessments should provide information which permits risk managers to compare alternatives."

EFED Response

The RED examines effects at different points in the distributions of important variables considered and EFED has asked Syngenta to include components such as sensitivity analyses in its submissions. Discussions are currently taking place with regard to risk management options available, and EFED's work examining the risks of alternatives will be key.

Syngenta Comment

"Selective Use of Existing Toxicity Data Results in an Incomplete Risk Assessment
A large quantity of valid, relevant ecological information has been unnecessarily excluded from the EPA assessment. Nearly 200 plant and animal studies were included in the refined risk assessment for atrazine submitted by Syngenta (Giddings et al., 2000)...the EFED assessment relies on the lowest values available, in nearly all cases, for plants, invertebrates, fish, birds and mammals. This approach distorts the estimated risk and does not permit reliable predictions of risk to be made...Similar limitations in the use of field data exist. The EPA assessment of atrazine relies heavily upon the results reported by Kettle et al., (1987), to support the prediction of reductions in macrophyte plants at 20 µg/L and to extrapolate to subsequent indirect impacts on fish populations...As described in detail in our response, this study is of limited value and the data are not reproducible...Numerous studies, conducted much more recently than Kettle et al., (1987), which indicate no effects on phytoplankton, periphyton and/or macrophytes at concentrations as high as 100 µg/L (Appendix 1). No effect levels for other studies are even higher when rapid system recovery is considered."

EFED Response

EFED acknowledges the comprehensive literature search and compilation of ecotoxicology laboratory data gathered by the Panel and presented in Tables 5.1 to 5.4, as well as the mesocosm and microcosm data presented in Tables 6.1and 6.2 from Giddings et al 2000. EFED also acknowledges the detailed analysis of the monitoring data presented in Appendix 6 of "Syngenta's Comments in Response to the Notice of Availability of Environmental Fate and Effects Assessment on Atrazine to Re-registration Eligibility Decision" [OPP-34237A]. EFED commends Syngenta and the Panel for this effort which is more comprehensive than the data presented in the Agency's Re-registration Eligibility Science Chapter for Atrazine, Environmental Fate and Effects Chapter [OPP-34237A]. The Agency will include this additional ecotoxicological laboratory and simulated field data, as well as the analysis of the monitoring data, by reference in its updated Science Chapter for Atrazine. While the Agency still has concerns for adverse effects on aquatic communities from the continued use of atrazine, the additional information presented by Syngenta and its Panel will help the Agency refine the magnitude and likelihood of these effects. The Agency has expressed serious reservations concerning conclusions reached by the Panel's probabilistic risk assessment for atrazine due to the methods used for both the distribution of the effects and fate data, as well as the index of risk. Consequently, the Agency has not included any of this information in its updated Science Chapter. These concerns are found in the attached document "Review of Atrazine PRA."

Syngenta Comment

"There is a Lack of Evidence for Aquatic and Terrestrial Indirect Effects
The RED places great emphasis on the unlikely possibility of indirect effects of atrazine on nearly all components of aquatic and terrestrial ecosystems, including invertebrates, fish, birds and mammals. These indirect effects are incorrectly assumed to occur as a result of atrazine impacts to aquatic and terrestrial plants. While this is theoretically possible, these effects are not expected at the concentrations and exposures stated by EPA or anticipated in the environment.

The EFED assessment presents three field studies as endpoints for fish and invertebrates to support the conclusion of indirect aquatic effects. However, these studies have been characterized as questionable due to design weaknesses such as lack of replication and lack of controls, lack of consideration for possible confounders, or for reporting inadequacies that do not permit evaluation of methods and results. Furthermore, the results relied upon in the RED to conclude indirect aquatic effects, are inconsistent with the weight of evidence provided in numerous, higher quality microcosm and mesocosms studies in which effects on invertebrates are not reported at similar concentrations.

The premise that atrazine is causing off-target terrestrial plant damage, leading to indirect animal impacts is not supported by scientific studies."

EFED Response

The Agency considers the reported results of the field studies in question as indicating potential adverse effects, both direct and indirect, on aquatic communities from the use of atrazine. The results from these field studies, while containing methods and approaches which are not in complete compliance with the EPA Mesocosm Guidance published in 1998, still raise valid risk concerns. The Agency's reviews of these studies and their utility are found in the attached document "Review of Atrazine PRA." Further, the studies in question were completed well before the Agency guidance was published.

From the Agency's perspective, the primary issue is what is the likelihood and magnitude of adverse effects from the continued use of atrazine. It is noted that atrazine has been widely used for more than 40 years, and any adverse effects are likely to have impacted the aquatic environment already. The additional information on laboratory and simulated field ecotoxicological data as well as the analysis of the monitoring data provided by Syngenta and its Panel has helped the Agency update and further refine its Science Chapter.

Syngenta Comment
"...Considering that approximately 519 million acres of corn received atrazine applications in the U.S. during the period considered by the EPA (1991 to 1999), 14 potentially reliable but unconfirmed incident reports represents an extremely low frequency and number."

EFED Response

The Agency believes that incidents can be used to show that there are impacts from the regular use of a pesticide, and as such are reflective of the fact that chemical-specific effects on nontarget animals or plants are being observed in the field. In concert with the quotient assessment and with field studies, they help provide a picture of the risks and impacts that can result from the use of the pesticide. A more detailed discussion is included below.

Syngenta Comment

"Limited Use of Exposure Monitoring Data Results in Incomplete Exposure Characterization
Although the EFED assessment provides plots of the distribution of selected data, EFED relies almost exclusively on maximum values recorded per location or year and on distributions of the maximum values. In many cases, they state that the data are too limited to provide an adequate time series, so they focus on the maximum values. In contrast, for sites with limited data, Giddings et al. (2000) used exposure distributions reflecting the 90th percentile concentration for each site. These distributions provide a better representation of the upper end of exposure than do maximum values alone."

EFED Response

In the case of "limited" and "incomplete" monitoring data, it is not clear at all that distributions of the "90^{th} %ile" values provide a better representation of upper end exposure than do the maximum values observed. In fact, a strong argument can be made for using maximum observed values to represent upper end percentiles, especially when datasets are small. Smaller samples have far lower probability of including the "true" maximum or even the "true" 95^{th} %ile of the population of concentration values in a given area, and there is far less precision around the estimates than with larger samples. Therefore, questions of whether or not the "90^{th}" %ile value of limited data represents the 90^{th} %ile of the "true" distribution, and whether the maximum observed value approximates the "true" maximum become much more important with limited data. Clearly, the maximum observed value in any sample can only provide a lower bound on the "true" max of the population. That is, the true max is always equal to or greater than the maximum concentration found in any sample.

In cases where there is a steep drop in the data from 100^{th} %ile down to the 90^{th} %ile, for instance, the 90^{th} %ile value may be much more representative of the lower end of the distribution than the upper. In the NAWQA data of positive values as presented by Syngenta, there is over a 10-fold difference between the second highest value of 27 ppb and the 90^{th} %ile value of 1.9 ppb for the dataset. The highest value in the sample, 120 ppb, is 60 times the 90^{th} %ile value. Syngenta has used the term "outlier samples" for these samples. While this highest value may far exceed a large number of the combined samples, it is not "an outlier" for its particular dataset. All laboratory values in the NAWQA program are confirmed, and the sample findings represent actual concentrations that are possible under real environmental conditions. When considering acute endpoints, these highest concentrations are those that most warrant the Agency's attention, rather than dismissal. Lower values more representative of the entire distribution may be considered in conjunction with chronic endpoints.

Thus, as discussed further in the section on NAWQA data in this document, EPA believes that the type and location of the samples collected are important for performing separate analyses that will better characterize the levels in certain locations or types of areas, as well as point out potential avenues for mitigation. Finally, in USGS survey data segregated for post-application and presented in the RED, even the 90^{th} %ile values were in the 20-40 ppb range.

<u>Syngenta Comment</u>

<u>"Limited Use of Exposure Modeling Data Results in Incomplete Exposure Characterization</u>
The approach to exposure modeling employed by the EPA is consistent with the lower tiered, deterministic approach of screening level assessments... refined modeling was conducted as part of the probabilistic assessment (Giddings et al., 2000)...It is important to note that the highest concentrations [Syngenta] modeled were consistent with those of the lower tier estimates of the EPA. However, information on the range of values in the distribution and the likelihood of occurrence is also provided, resulting in the ability to quantify the probabilities of various exposures. The advanced modeling employed in the probabilistic assessment remains conservative and numerous refinements to better reflect actual use scenarios are possible. The refined modeling recommendations of ECOFRAM are consistent with the scientifically appropriate probabilistic exposure refinements for atrazine."

<u>EFED Response</u>

EFED relied in part on Tier II model-estimated environmental concentrations, and the models used in the process (PRZM/EXAMS) have been subject to considerable scrutiny, with their field-based performance coming under continual evaluation.

Syngenta's assessment utilized the Multiple Scenario Risk Assessment Tool (MUSCRAT) to facilitate a batch run and statistical analysis of exposure scenarios evaluated with PRZM/EXAMS. A fully functional, well-documented version of the MUSCRAT model is not yet in place for routine use in OPP, however, although EPA did participate in the development of MUSCRAT. Furthermore, EFED had concerns about the use of the "crop-climate-soil" combinations or "bins" constructed by the registrants, which lacked some transparent documentation and are subject to much discussion about the appropriateness of definition and aggregation both. Finally, the RIVWQ model has not been tested, used or validated in OPP, and little if any discussion has occurred among the staff.

In many cases the "conservative" Tier II PRZM/EXAMS EEC predictions have either coincided with monitoring data or have actually underestimated the concentrations found in monitoring from streams or reservoirs. EFED's PRZM/EXAMS predictions for sugarcane, for example, reached a peak of 205 ppb and averaged 194 ppb for 90 days. Monitoring data from the Upper Terrebonne watershed around sugarcane crops ranged from 210 ppb to 216 ppb for the top 5% of the samples. A similar situation exists for both corn and sorghum, where actual monitoring data exceed the predicted peaks of ~38 ppb and ~73 ppb, respectively.

p.21-23 S**yngenta General Comments on Assessment Procedures**

p. 21. **Syngenta Comment:** *"The lower tier assessment [EFED risk assessment using monitoring data for atrazine exposures, as compared to industry's Atrazine Probabilistic Risk Assessment (PRA)], inaccurately concludes that atrazine exposure 'has serious implications when compared to ecotoxicological endpoints of concern' and erroneously predicts impacts on nearly all aspects of the ecosystem: mammals, birds, fish, invertebrates, and non-target plants. Misinterpretations lead to the statement that the 'most important environmental risk associated with atrazine are toxicological effects on freshwater and estuarine plants and their communities, as well as indirect effects on aquatic invertebrates and fish.'"*

EFED Response: The Atrazine Ecological Risk Assessment Panel failed to consider three parameters in their probabilistic risk assessment. First, they failed to consider the effects of prolonged atrazine exposures on aquatic plants. Second, the Panel addressed aquatic risks only for streams and rivers (i.e., only flowing waters). Third, the PRA can not address indirect effects. The Agency agrees that acute risks to birds and mammals and aquatic animals are not significant, if they are based on direct toxic effects from atrazine. Except in small rivers and streams in high atrazine use areas, serious adverse effects on aquatic plants and plant growth are unlikely to have serious effects in constantly flowing waters, because the exposure period is fairly short and the atrazine concentration is relatively low. Some plant recovery from atrazine in flowing waters may occur, but as one author found, atrazine-treated plants may never fully recover (Jones, et al., 1986).

Freemark and Boutin (1994) concluded that "Wildlife (including birds, mammals and their resources) are exposed to herbicides primarily through direct overspray, spray drift and vapour drift. Except for a few cases, vertebrate wildlife are unlikely to be exposed to herbicide levels that are acutely toxic. In contrast, herbicide use has induced changes in wildlife resources through a variety of effects on different taxonomic group species (e.g. plants, soil organisms, insects, other invertebrates). Coupled with field studies on birds and mammals, there is sufficient evidence to suggest that herbicide use has adversely affected wildlife, primarily through a variety of toxic effects on plants, and simplification in habitat composition, heterogeneity and interspersion." These indirect effects are difficult to predict and can not currently be assessed with PRA.

The major point of the Agency's aquatic risk assessment, which the Risk Assessment Panel has not adequately addressed, is the indirect effects on aquatic animals from changes in the vegetation resulting from prolonged exposure of aquatic plants to 10-20 μg/L atrazine. A number of aquatic studies were cited in the Agency risk assessment, which indicates that oxygen production is reduced at levels as low as 1 ppb of atrazine. Oxygen production is a reflection of a plant's ability to produce food. In small rivers, streams and non-flowing surface waters, atrazine has a longer residence time and will continue to adversely affect the ability of aquatic plants to photosynthesize and grow for a long period of time. The starvation of the plant will continue as long as the atrazine concentration exceeds the toxicity value for the functioning of the photosynthetic process. With an estimated mean aquatic half-life of about 159 days, 10-20 μg/L atrazine will persist a long time before reaching the 1μg/L concentration that blocks photosynthesis for a number of aquatic plants.

The PRA assumed that the exposure times would be relatively short and they did not address effects on plants from prolonged exposures, because their model only addressed flowing waters. Their PRA did not address risks to aquatic areas with longer water retention periods, such as lakes, farm ponds, marshes, swamps, intermittent streams and confined estuarine areas. It was under these conditions in Kansas ponds that DeNoyelles, Jr., Kettle and Sinn 1982 (phytoplankton); Dewey 1986 (insects); Kettle, DeNoyelles, Jr., Heacock and Kadoum, 1987 (vegetation, juvenile fish and insect prey) tested atrazine at 20 and 500 μg/L in 0.045 hectare ponds. A series of different tests over several years showed effects on different parts of the aquatic community affected by a single application of 20 μg atrazine per L sprayed directly to the surface of ponds. Macrophytes were affected over a period of months and a year. The losses in the biomass of the aquatic macrophytes reduced the protective habitat that aquatic plants provide juvenile fish, small fish species and non-infaunal benthic insect populations. Population shifts occurred in phytoplankton from sensitive to resistant species. Benthic insect populations and levels of emergence of the chironomid *Labrundinia pilosella* were significantly reduced. Bluegill young were reduced by 95 percent and insect levels in fish stomachs were significantly reduced in number and species richness. These effects on zooplankton, insects and young and adult bluegills were the result of **indirect effects** from the loss of aquatic vegetation from 20 μg/L of atrazine.

p. 22 Syngenta Comment: *"The EFED's lower tier (Tier I/ Tier II) assessments rely primarily on the extreme, worst case toxicity data available, the maximum exposure values available and hypothetical assumptions on indirect effects on wildlife which have not been substantiated in numerous field studies.*

EFED Response: EFED's risk assessment was as refined as data allowed. The tiered risk assessment approach, which was not followed by the Panel, begins with conservative exposures and toxicity values while subsequent tiers focus on areas where risks exist, using more refined values in each tier. Tier I for the aquatic estimated environmental exposure concentrations (EECs) is supposed to be based on the GENEEC Model. EFED began Tier I with the EECs from PRZM-EXAMS Model, which is normally the Tier II refinement. The conclusions from EFED's Tier I assessment were that the acute risks to wildlife were low for all taxonomic groups except terrestrial and aquatic plants. There were some possible, moderate reproductive effects for mammals, birds, fish and aquatic invertebrates. However, the major effects and area of greatest concern in Tier I appeared to be aquatic plants. The problem formulation for Tier II, therefore, was to address the high risks to aquatic plants.

The direction for the Tier II assessment was to refine the aquatic exposures with realistic aquatic EECs derived from monitoring data. The atrazine risk assessment was one of the first times that national monitoring data were used to assess risks to aquatic life. Distributions of atrazine concentrations were created from a number of data bases. These monitoring distributions were compared to a broad data base of aquatic vascular plants and algae, as well as the results from microcosms, mesocosms and field studies. The largest data base for field studies came from a series of Kansas pond studies which showed significant effects on macrophytes and indirect effects on a wide-spectrum of species in the aquatic community. The direct effect on macrophytes at 20 μg/L atrazine were dramatic, with 60 to 90 percent reductions after 6 months and 1 year, respectively.

Indirect effects on young bluegill survival and some insect populations and chironomid emergence were equally dramatic at 20 μg/L.

Problem formulation for Tier III was difficult because insufficient toxicity data were available to assess risks to aquatic plants for different exposure durations. The aquatic EECs were already as refined as they could be since they were based on monitoring data. And there currently are no models to assess the risks from indirect effects. From the field data that existed, EFED could not estimate the level of no concern for adverse effects on aquatic plants, fish recruitment or insect populations and emergence which could occur as indirect effects. There were additional issues on risks to consider, but there was no methodology to address the refinement of the risks.

p. 22. **Syngenta Comment:** *"A more realistic risk assessment must consider and account for 1) the exposure concentration distributions, 2) the species sensitivity distribution, and 3) seasonal exposures variations. There are sufficient amenable monitoring data and toxicity data available for OPP to conduct a probabilistic aquatic risk assessment for atrazine."*

EFED Response: The acute risks for flowing waters were minimal, except for aquatic plants. As indicated above, there was inadequate plant toxicity data to a assess varying time exposures. And none of these parameters can be related to the refinement of the indirect effects which were found ponds at 20 μg/L.

p. 22. **Syngenta Comment:** *"The EPA has stated that the large amount of ecotoxicological data and monitoring data available for atrazine is not appropriate for probabilistic analysis."*

EFED Response: As discussed above, acute risks to aquatic ecosystems were found to be marginal in flowing waters. The areas of major concern for adverse effects were lentic habitats. Where aquatic plants were exposed to atrazine for long periods of time, the loss of aquatic vegetation caused significant indirect effects on fish and aquatic invertebrates. In spite of the large amount of ecotoxicological data available, those data are not applicable to assessing risks from indirect effects. If there are predictive PRA models available for assessing risks from indirect effects, EPA would be willing to discuss and evaluate the model(s).

p. 23. **Syngenta Comment:** *"However, EFED, with exception of the questionable Kettle et al. (1987) study, did not appear to utilize any of the other mesocosm studies to characterize risk for aquatic plants, fish or invertebrates."*

EFED Response: The goal of tiered risk assessment is to identify areas of concern found at one level and focus with more precision on that concern at the next tier level. EFED reviewed a number of mesocosm studies and some studies reported adverse effects at atrazine levels as low as 10 μg/L. Emphasis was placed on the Kansas pond studies, however, because the effects in those studies were more serious than those reported in all the other studies. With respect to the validity of the Kettle *et al*. study, Kansas pond studies were conducted by several authors over a period of several years and have shown effects on almost all taxonomic groups in the aquatic community at 20 μg/L. Except for the effects on fish stomach contents and fish recruitment, which have not been studied by the other authors, the results on vegetation loss and reductions in insect populations in the Kettle study were consistent with the results of one or more of the other Kansas studies.

p. 24 **Risk Management Implications and Comparative Risk of Alternatives**

Syngenta Comment: *"The current EFED assessment for atrazine fails to provide the precision necessary for useful risk management decisions..."* and *"For appropriate risk management decisions to be made, accurate comparisons between alternatives is needed."*

EFED Response

EFED performed the most refined risk assessment possible with available data. The risks and uncertainties that have been identified will be considered in any risk management decision. In addition, the updated RED chapter released for public comment will better identify endpoints and will include a comparison of the risks posed by alternatives to atrazine.

p. 25-31 **Terrestrial Birds and Mammals and Non-Target Plants**

p. 25. **Syngenta Comment:** *"The reproductive NOAEL stated to be 10 ppm based upon body weight effects in the pups of a second generation rat reproduction study (MRID 40431303) is incompatible with the pup NOEL reported by OPP (Table 8.1, page 69< Toxicological Chapter of the Revised RED for atrazine January 18, 2001). ... Therefore, risk quotients for mammals should b based on 50 ppm."*

EFED Response: The HED TOX ONELINER (dated 11 Aug. 1999) cites the results from a 1987 2-generation rat reproduction study submitted by Ciba Geigy Pharmaceutical, England. The TOX ONELINER clearly reports "Reproductive NOEL = 10 ppm. Reproductive LEL = 50 ppm based upon decreased body weights of pups of the second generation on postnatal day 21. Review of the DER (# 006937) verifies the conclusions reported in the ONELINER. Since effects on pup body weights were reduced at 50 ppm, it would be inconsistent with Agency policy to use this concentration as a NOAEC for risk assessment.

p. 26. **Syngenta Comment:** *"Several foliar half-life values stated by EPA on page 62 of the RED are erroneous. An Atrazine turf dissipation study in Florida and Georgia (MRID No. 449588-01) indicates the half-life ranged from 4.9 to 6.9 days without irrigation and was 6.5 hours with irrigation, not 6 days as stated in the RED."*

EFED Response: EFED used the more conservative foliar half-life of 17 days reported for turf in Georgia (MRID 449580-01). This is not an error.

p. 26. **Syngenta Comment:** *"Syngenta has also examined residue reports following application of atrazine to rangeland grass at application rates of 2 to 4 lbs a.i./A. Six trials were relevant to a risk assessment as they contained initial measurements (immediately following application) and residues were analyzed from green grass forage. The average initial concentration from the 2 lb* *a.i./A application was 147 ppm (range: 38 - 286 ppm) and the average concentration following the 4 lb a.i./A application was 343 ppm (range: 190 - 486 ppm). These residue values are much lower than those predicted by the EPA's screening level exposure model and once again indicate there is no risk to terrestrial animals from realistic exposure."*

EFED Response: EFED uses standard residue values for exposures of birds and mammals. The original values were recommended by Hoerger and Kenaga (1972) of the Agricultural Dept., Dow Chemical Corp. for "estimation of their magnitude [pesticide residues on plants] in the environment." These recommended residue levels were derived from a large data base compiled from the literature and from United States crop tolerances. The residue values were reviewed by Fletcher *et al*. (1992) with little change. Residues were identified for maximum residue levels and mean residue levels for short (wheat) and long grasses (tall crops), foliage (leaves) and fruits and vegetables. Refined risk assessments may consider other residue data, but refined assessments require the availability of many data points on the particular chemical. Acute risks for atrazine to birds and mammals were not sufficient to trigger a refined risk assessment.

p. 26. **Syngenta Comment:** *"Preplant applications with conventional tillage: The majority of weed foliage and seeds would be buried the soil surface and unavailable to wildlife. Incorporation of atrazine will further minimize exposure."*

EFED Response: EFED recognizes that soil incorporation of weed foliage and seeds reduces the amount of food available to wildlife, but it does not reduce the atrazine levels on the vegetation exposed above the soil surface. While it may be harder to find, the vegetation retains the same concentration of atrazine. Furthermore, it may take days after application for plants to become unpalatable, as indicated in a subsequent comment.

p. 27. **Syngenta Comment:** *"An absence of weeds in the treated field also results in minimal abundance of weed seeds and insects that associates with these plants. The only green vegetation of significance in the treated field will be the crop where residues rapidly decline."*

EFED Response: First, soil incorporation reduces the number of seeds and the amount of vegetation present on the soil surface, but soil does not cover all treated-seeds and vegetation. Soil incorporation reduces and limits wildlife resources, but it does not prevent wildlife exposure to atrazine on food items remaining on the soil surface in treated fields. The reduction in wildlife resources by herbicides and soil incorporation supports the conclusions in the last paragraph in the "Animal Risk Assessment" section of the Agency's Atrazine RED. When the resources that wildlife depend on for food (i.e., mostly seeds), cover, nesting and/or brood-rearing survival are diminished, the animals must move to other areas which are generally less favorable than the habitat that they had occupied before herbicide treatment.

p. 27. **Syngenta Comment:** *"In summary, these points illustrate that potential for exposure in the treated field is minimal and there is high certainty that 100% of the animal's diet could not come from the treated field over an extended time."*

EFED Response: There is no need for wildlife to feed on treated areas for 100 percent of their food in order for effects to occur if exposure is greater than toxicity levels. For example, if residues on vegetation were 400 ppm and the toxicity value was 200 ppm, the diet would only have to average 200 ppm. Hence, the animal could consume 50 percent of the food outside of the treated area.

With respect to length of exposure periods for chronic effects on animals, there are two areas of uncertainty. Not all corn fields are treated at the same time, so wildlife may move from one treated-corn field to another as long as seeds and insects are available and the vegetation is palatable. Second, there is considerable uncertainty about chronic effects with respect to the timing of the exposure and how long the exposure takes to produce a chronic effect. Test data are not available to answer these last questions for atrazine and many other pesticides. Hence, Agency policy does not require chronic exposures to invoke concern for chronic effects. For atrazine, the chronic endpoint for birds and mammals is body weight loss or reduced body weight gain. The loss of favorable habitat and increased competition with other animals for food are also likely to affect body weight, if food sources are in short supply. These indirect effects on wildlife from mono-culture cropping and the loss of wildlife resources are the same for any herbicide. Therefore, it is more important to focus on those effects which are particular to atrazine and may have a significant impact on the environment.

p. 27. **Syngenta Comment:** *"Finally, EPA makes statements that habitat alteration by herbicides renders it no longer suitable for wildlife species. They state that alteration in types of vegetation or reduction in food sources within the habitat will result in the animal moving elsewhere to a less suitable area."*

EFED Response: As stated above in the Syngenta comments, when atrazine is soil incorporated, the amount of seeds and vegetation are reduced and about one week after treatment the vegetation is unpalatable. This loss of wildlife resources (i.e., food and cover) forces wildlife to seek other suitable areas. Corn fields are prime habitat for many wildlife species. According to Gusey and Maturgo (1973), wildlife utilization of corn is higher and by a broader range of birds and mammals than any major crop in the US. When the resources that these wildlife depend on for food (i.e., mostly seeds), cover, nesting and/or brood-rearing survival are diminished, the animals must move to other areas which are generally less favorable than the habitat that they had occupied before the herbicide treatment. The citation for the reference on effects of habitat change on wildlife population and their movement to less favorable habitats was added to the RED (i.e., Freemark and Boutin, Canadian Wildlife Service, 1994).

p. 28. **Syngenta Comment:** *"In summary, the EPA's terrestrial assessment is incorrect: there is no indication of risk to birds and small mammals from atrazine use. The risk assessment should be based on all of the scientific information available and conclusions should consider factual information regarding agronomic practices and agro–ecosystem characteristics"*

EFED Response: EFED has found no justification for changing the Agency's risk assessment for mammals and birds. The monograph used to estimate residue data is based on "all of the scientific information available," not one limited atrazine residue study on grasses. The mammalian chronic toxicity value (i.e., NOAEL 10 ppm for rat pups) differs from the value used by human health scientists, but it remains a valid toxicity endpoint. Contrary to comments on the availability of food in atrazine-treated fields, some seeds, vegetation and insects remain exposed on the soil surface after soil incorporation. Treated vegetation remains palatable for at least a few days after treatment. When wildlife resources in the favorable habitat are insufficient, the animals move, generally, to other less favorable areas than those they selected before herbicide treatment. All components of the terrestrial wildlife risk assessment remain unmodified; therefore, the risk conclusions for terrestrial wildlife are unchanged.

Comments on Non-Target Plants:

p. 28. **Syngenta Comment:** *"The EC_{25} represents a sublethal endpoint (in studies conducted with atrazine a decrease in length or weight of the plant is observed) where plants can recover."*

EFED Response: The EC_{25} terrestrial plant endpoint is based on a reduction in shoot length and dry weight, as stated. While Syngenta has claimed that "plants can recover," they have not provided test data that demonstrate that with these growth effects, plants will recover. Also Syngenta has not shown that following any recovery from effects on growth, there is not still an adverse effect on crop yield.

p. 28. **Syngenta Comment:** *"The exposure scenarios do not assume any degradation, infiltration to the soil, or structural interception."*

EFED Response: The exposure scenarios do not assume degradation because the plants were tested under conditions similar to field conditions for spray drift. The seedling emergence test differs in that the test plants were watered from the bottom, which corresponds to the comment about soil infiltration. Structural interception would not appear to be a problem for pre-emergent ground applications.

p. 29. **Syngenta Comment:** *"There is a large discrepancy in modeled exposure and exposure simulated in the toxicity studies. In the vegetative vigor study, drift is not simulated-rather, plants are directly over-sprayed at the field application volumes resulting in complete coverage."*

EFED Response: Theoretically, the test plants are directly sprayed with 100 percent of the field application volume. The simulation assumes only 1 percent drift rather than 100 percent and the toxicity values are adjusted accordingly. There is no requirement that the entire plant be treated to produce adverse effects. Only three crops were estimated to be moderately affected from spray drift following a ground application (i.e., risk quotients ranged from < 0.01 to 8). Risk quotients for non-target seedlings ranged from 0.63 to 310 and up to 370 for endangered plants.

p. 29. **Syngenta Comment:** *"Young sensitive plants are used to represent the sensitivity of all plants. Atrazine efficiency shows that young plants are more sensitive than more mature plants."*

EFED Response: The use of young plants is particularly appropriate for herbicides applied pre-plant or anytime during the spring when many non-target species have just sprouted.

p. 29. **Syngenta Comment:** *"The risk assessment assumes that laboratory generated effects equal effects observed in the field. Laboratory grown plants are generally more susceptible to herbicide injury than field 'hardened' plants. Plants grown in the laboratory are subjected to few environmental stressors due to lower light intensities, higher and more uniform humidity, more uniform temperatures, and lack of wind. These relatively constant conditions can cause plants to produce foliage with thinner cuticles and wax layers, which in turn reduces this barrier to external effects and allows for increased chemical uptake. Wright and Thompson (2001) have summarized a number of studies comparing greenhouse to field trials which indicate that greenhouse studies can over-predict field results from 30 to 90%. Additional studies also indicate this difference in laboratory to field extrapolations (Harrison et al. 1998)."*

EFED Response: It is desirable that the plants tested in greenhouses are healthy and are not under stresses from any other source than the test chemical, in order to determine the inherent toxicity of the test substance. If a herbicide is applied to plants in the field that are under stress from drought, for example, the added exposure to another stressor is likely to enhance the adverse effects on the plant. Many pesticide labels have warning statements recommending not to apply the product when plants are under one stress or another. There are many environmental factors that can increase as well as decrease the toxicity of a pesticide to plants. The risks of concern for atrazine are from effects on seedling growth, a soil exposure, rather than from spray drift, a foliar exposure. Hence, the cuticle thickness and wax layers are marginally important for atrazine.

p. 29. **Syngenta Comment**: *"Use of atrazine is important for vegetation management in conservation programs. However, EPA has not defined what non-target plants should be protected in agro-ecosystems. This should be done at the outset of the risk assessment."*

EFED Response: Herbicides are registered for specific use sites (e.g., field crops, right-of-ways, forests). Any vegetation which exists outside the treatment area is considered to be a non-target plant. Vegetation and areas of particular concern for herbicide effects are buffer strips, riparian habitats, endangered plant species, as well as other non-target field crops. The Agency assessment of vegetative risks made in the Atrazine RED is for all non-target plants found adjacent to treated areas.

p. 30-31. **Syngenta Comments on Incident Reports**: *"Closer inspection of the summary list of 35 highly probable/probable plant cases reveals the EPA's assessment is in error:*

- *Six cases were labeled as misuse/accidental.*
- *One runoff report was from an atrazine/cyanazine treated field and cannot be solely attributed to atrazine.*
- *Sixteen cases were associated with corn and 14 of these were submitted by Syngenta (formerly Novartis) in 1999 following Bicep application (a combination of atrazine and metolachlor). Syngenta examined the 14 cases cited in the RED and determined that since two compounds were allegedly involved in the incident and the injury was due to factors*

other than atrazine (determined by Syngenta's Technical Service group), the EPA statements are not accurate.

- *Only 14 plant incidents could possibly be attributed to atrazine.*

EFED Response: Syngenta stated on page 29 that "The RED inaccurately concludes adverse effects are occurring to non-target plants," but concluded that atrazine effects could be possible on page 30 (i.e., "Only 14 plant incidents could possibly be attributed to atrazine."). According to the registrant, atrazine was not responsible for any adverse effects when the incident was due to misuse or when atrazine was present with one or more pesticides. When two or more chemicals are present, Syngenta has assumed without quantification of risks that atrazine provided no toxicity and that there is no joint toxicity.

EFED agrees that other herbicides may have contributed to the incidents and that atrazine is tank mixed with many other chemicals. Metolachlor and Bicep, for example, may be more toxic than atrazine, but that does not remove atrazine as a potential contributor to joint toxicity. In addition, misuse and accidents unfortunately do occur, and they reflect real ecological risk from pesticide registration. We are in agreement, at least, concerning the 14 atrazine incidents.

p. 30. **Syngenta Comment**: *"Atrazine is not toxic to fish or birds, therefore the EPA conclusion that incidents involving fish or birds may be attributable to atrazine are inappropriate. Based on studies demonstrating the safety of atrazine to fish and other vertebrates, and on a wealth of published and unpublished data, it is highly unlikely that atrazine contributed to the effects seen."*

EFED Response: It is unclear what studies demonstrate the safety of atrazine to fish and other vertebrates. Toxicity studies submitted on fish and wildlife indicate the level of toxicity of a chemical to fish and wildlife. There is no assessment of risks or conclusions of "safety" in these studies.

Toxicity studies indicate that atrazine is toxic to a number of fish species both acutely and chronically. The EPA risk assessment suggests that atrazine uses do not pose an acute risk to fish and that chronic effects are moderate (i.e., chronic risk quotients for sugarcane at 4 lbs ai./A were 2.9-3.1). The exposure models used in this risk assessment, however, while not predicting high risk, might also underestimate exposure under certain conditions.

EFED clearly expressed in the section on "Reported Ecological Incidents" that the cause of the fish kills was unknown. Many fish kills occurred during the spring rains after atrazine application. Some plausible explanations were offered, but no causality was established. Whether atrazine affected the fish directly or indirectly from low dissolved oxygen levels, or had no responsibility, is unknown. The reason for these fish kills remains an uncertainty.

p.32 **Syngenta Comments on Atmospheric Deposition**: Syngenta presented a long description of EFED's assessment of possible adverse effects from atmospheric concentrations of atrazine in rainfall.

EFED Response: EFED made a cursory risk assessment of atrazine concentrations in rainfall. The highest atrazine concentration in rainfall was reported as 3.5 μg/L in Germany. EFED made some preliminary calculations based on plant toxicity values for vegetative vigor and seedling emergence and concluded that atrazine did not pose a risk and that "aerial deposition of atrazine at concentrations up to 50 μg/L would not appear to be a risk to birds, mammals, fish, aquatic invertebrates and aquatic vascular plants. ... Based on the NOAEC values for risks to endangered species, a rainfall event with an atrazine concentration of 50 μg/L would exceed the level of concern of 44 μg/L using the most sensitive vegetative vigor, NOAEL value (i.e., 0.005 lbs ai/A) for cucumbers and cabbage." Since the highest atrazine concentration in rainfall was 3.5 μg/L, which is well below 44 μg/L, **atrazine levels in rainfall do not pose a risk to endangered plant species.**

p. 34 **Syngenta Comments on Endangered Species:** *"The EPA risk assessment inaccurately indicates that terrestrial plant endangered species are likely to be affected and wildlife species may be indirectly affected by atrazine use. This broad statement is used consistently throughout the document with no scientific data supporting this claim. This statement is apparently a result of the non-target plant risk assessment which indicates potential risk to non-target plants based on unrealistic exposure and toxicity assumptions. In addition, the risk assessment is not substantiated by incident reports. There is no evidence to suggest atrazine has caused wildlife habitat loss or resulted in the indirect effects alluded to in the RED despite more than 40 years of continuous use."*

EFED Response: The section on "Summary of Risk Assumptions" explains how the Risk Quotients are calculated from the EECs and toxicity values, and explains what Risk Quotient level serves as the Level of Concern (LOC) for each taxonomic grouping. For terrestrial plants, the toxicity values are EC_{25} and EC_{05} or NOAEC for acute risks and acute endangered species risks, respectively. For all terrestrial plants, the LOC is a risk quotient of 1 for non-target plants. The determination of risks to terrestrial plants is consistent with the finding of incidents of adverse effects on plants reported by Syngenta.

EFED stands by its methods of plant risk assessment, and continues to work to improve its methodology. A peer review of the standard EFED risk methodology is anticipated for the Science Advisory Panel in the Spring of 2003. No research has quantified the extent to which atrazine may have caused wildlife habitat loss or resulted in indirect effects over the last 40 years. By continuous improvement of methodology, EFED will continue to fulfill its mandate to produce high quality pesticide risk assessments.

p. 35-40 **Effects Characterization**

p. 35. **Syngenta Comment**: *"A major advantage of the probabilistic techniques is that they use all relevant single species toxicity, rather than relying on a few species to represent the range of species found in the environment."*

EFED Response: As discussed above, the PRA can not be used to assess indirect effects. PRA can not extrapolate plant toxicity levels for exposures which are longer than the test period of 4 to 30 days, and PRA can not predict nor quantify indirect adverse effects. The indirect effects identified by the Agency occurred at an atrazine concentration of 20 μg/L. This was below the toxic concentrations identified from single species tests, because atrazine risks to plants are time dependent. The longer the atrazine concentration exceeds the compensation point at which a plant produces more energy than it consumes, the plant will feed on its energy reserves until no energy reserves are left and the plant dies. Lentic habitats provide conditions under which atrazine concentrations can remain at levels higher than the compensation points for some aquatic plant species until they die. The Agency is receptive to the submission of a methodology to quantify risks from indirect effects.

p. 35. **Syngenta Comment**: *"As an illustration of EFED's overly conservative use of the available toxicity data, Figure 1 provides the distributions of toxicity values for aquatic plants which were considered accurate and valid for the probabilistic risk assessment (Giddings et al. 2000)."*

EFED Response: For atrazine the selection of "accurate and valid" toxicity values for aquatic plants is qualified by a time component, and any toxicity value must be specified by the time of exposure to atrazine. This time dependence can be seen in the toxicity data for *Lemna gibba,* with toxicity values at 5, 7 and 14 days. There are no data for other aquatic plants with multiple toxicity values under similar conditions for different time periods. The toxicity values for *Lemna gibba* are as follows: 170 μg/L for 5- and 7-day tests and 37 and 43 μg/L for 14-day tests.

p. 36. **Syngenta Comment**: *"In its current assessment, EFED has chosen a value of 1 μg/L(Torres and O'Flaherty, 1976) for predicting chlorophyll production impacts from atrazine to plants. This value is less than the first centile on the distribution and therefore does not [sic] the typical or widespread responses of plants to atrazine. Furthermore, the effect of chlorophyll production is a non-standard endpoint inconsistent with the mode of action of atrazine. Based upon this value, the EPA concludes widespread reductions on primary production by plants due to atrazine exposures. The value of such an assessment based upon extreme data is questionable and not substantiated by all of the available data."*

EFED Response: Torres and O'Flaherty reported reduction in chlorophyll effects at 1 μg/L on five single-cell algal species from three families. Chlorophyll production is a sublethal effect, which is a non-standard endpoint, but there is no Agency policy limiting the assessment to standard endpoints. To recognize sublethal effects even though they are non-standard is to include "all of the available data" in a risk assessment.

A number of other authors also have reported sublethal effects on aquatic plants as low as 1μg/L (e.g., O'Kelly and Deason, 1976; DeNoyelles *et al*., 1982; Lambert *et al*., 1989; and Bester *et al*., 1995).

p. 37. **Syngenta Comment**: *"In its assessments the EPA has used the lowest values available, in nearly all cases, for plants, invertebrates, fish, birds and mammals. The values selected not only the extremes of the distributions but in many cases highly questionable and unreliable data. Appendix I of the document contains additional comments relative to the selective use of toxicity data by the EPA."*

EPA Response: One goal of EFED's risk assessment is to protect biodiversity (i.e., risks to all species need to be considered). The lowest toxicity values are used as surrogate data to protect the large number of species which exist in each taxonomic group. It is well known that standard test species are not consistently protective of all species within a taxonomic group. Hence, the lowest toxicity values should not be considered "extremes".

Test results are called "highly questionable and unreliable" by Syngenta when there is not a second study to confirm the results of existing studies. The absence of confirmatory tests is not evidence that the original results are necessarily unreliable.

p. 37. **Syngenta Comment**: *"There are a large number of field microcosm and mesocosm studies available on atrazine which provide important information that should be used in a 'weight of evidence' approach to risk characterization. A detailed review of these studies, including those conducted at the University of Kansas, is available (Giddings et al., 2000). The approach taken by EPA in the atrazine aquatic risk assessment was to focus on two mesocosm studies Kettle et al. (1987) and DeNoyelles et al. (1982) for lentic system endpoints for fish, algae and plants. EPA did not utilize data from other mesocosm studies in their risk characterization. Not only did EPA focus on two studies but the studies chosen are scientifically inadequate to 'stand alone' in a risk assessment."*

EFED Response: The microcosm and mesocosm studies of importance to Syngenta's comment were not specifically cited. The microcosm and mesocosm studies reviewed by the Agency constituted short-term studies (i.e., mostly 2 to 8 weeks; only 1 study was tested for longer than 8 weeks). The 16-week study was conducted in an estuarine environment, which included tidal flushing that would dilute and carry away atrazine in ebbing tides. The Kansas pond studies were tested for 1 year with losses of atrazine limited to metabolism and other natural losses. As discussed above, the duration of exposure is an important variable causing adverse effects to plants. Atrazine studies were conducted at 20 μg/L several different times by a number of researchers. The authors and the areas where they found effects at 20 ug/L are as follows: Kettle *et al*. (1987) measured aquatic vegetation, fish young and insect levels in fish stomachs; and DeNoyelles *et al*. (1982) measured C-14 uptake, phytoplankton biomass and daphnid growth and reproduction. Dewey (1986) reported reductions in sensitive phytoplankton and insect populations at 20 μg/L atrazine.

p. 37. **Syngenta Comment**: *"EFED's inaccurate [sic] prediction of reductions in macrophyte plants at 20 μg/L with indirect impacts on fish population is a misuse of these data. The inferred effects at 20 μg/L reported in this paper were anomalous results that cannot be confirmed from the published data, were contradicted in another publication by the same researchers (DeNoyelles et al. 1982) and where not repeatable (Carney 1983)."*

EFED Response: Syngenta did not specify what the differences were between the test results reported by Kettle *et al*. and Carney. Carney (1983) is a MS thesis from the University of Kansas, which is not currently available for review. The title, "The effects of atrazine and grass carp on freshwater macrophyte communities" and Syngenta's concern about effects on fish in the Kettle study, suggest that atrazine may not have had the same effects on young grass carp as were seen with bluegill. If this is the difference that Syngenta wanted to identify, then there is a simple explanation. Grass carp are vegetarians and are therefore unlikely to feed on their young. Bluegill sunfish are carnivores and when their food sources are scarce they will feed on the young bluegill fry to survive. Grass carp were present in the Kettle study, but there was no evidence that the grass carp reproduced in the controls or in the treatments.

p. 37. **Syngenta Comment**: *"The EFED assessment's focus on endpoints from these publications in the absence of considering other studies is inappropriate for the following reasons:"* [Syngenta listed differences between EPA mesocosm guidance (Touart, 1988) and the methods used in the Kansas pond studies in a table].

EFED Response: The EPA guidance for mesocosm tests is a recommended test design for studies submitted by registrants to meet a data requirement. Since the Kansas pond studies were research studies and not submitted to support registration data requirements, there is no regulatory requirement to follow the test design. The Agency reviewed the peer reviewed, published studies and the Kansas pond studies were classified as supplemental for the lack of raw data. The absence of raw data in published studies is normal due to limitations on print space.

p. 39. **Syngenta Comment**: *"Despite these limitations [deviations from EPA test guidance], the finding is used in the panel's risk assessment, as a conservative measure, consideration of field effects. Giddings et al. acknowledged the observation by Kettle et al. of effects on macrophytes at 20 μg/L within a weight of evidence and probabilistic framework, but not as a reliable regulatory endpoint appropriate for deterministic assessments (Appendix 1) in their lower tier assessment. Similar to the above discussion on laboratory data, the EPA has chosen to ignore the more than 20 field microcosm and mesocosm studies available on atrazine."*

EFED Response: FIFRA requires a risk/benefit assessment for regulatory decisions. It is the responsibility of EFED to identify the risks to the ecosystem. In this case, the loss of aquatic vegetation is not the only endpoint of concern. There were indirect effects on the aquatic community including reductions in fish recruitment, insect populations, availability of food for bluegills and phyto- and zooplankton populations at 20 μg/L of atrazine.

p. 40. **Syngenta Comment**: *"Photosynthesis inhibition is the mode of action of atrazine in plants and is reversible. Plants recover rapidly after exposures to atrazine are reduced or eliminated. Atrazine inhibits photosynthesis by stopping electron flow in Photosystem II. This inhibition is reversible (i.e., it is algistatic not algicidal) over a wide range of atrazine concentrations. As noted by EFED in Jones et al. (1996) [sic, 1986], the recovery of oxygen evolution occurred within 2 hours at rates equal to the controls when the plants were placed into atrazine-free water. EFED questions the residual effects noted by the authors after 77 h, however, additional data on the rapid recovery are available."*

EFED Response: Reversal of atrazine effects on aquatic plants is not as simple as described by Syngenta. Jones *et al*. (1986) measured recovery of *Potamogeton perfoliatus* after exposure periods of only 2 hours. *Potamogeton* "was significantly inhibited by atrazine concentrations between 10 and 50 μg/L". Jones *et al*. reported that the recovery was rapid with plants reaching greater than 75% within 2-3 hours. Slower recovery occurred over the next 10 to 80 hours. "Even after 77 hours of flushing in the large volume experiment, mean photosynthesis was still less than control plants in the 100 μg/L treated plants." The measurement of photosynthesis was calculated as mg O_2/gdw/h. Jones *et al*. did not report the results for biomass for controls and treatments to confirm full recovery compared to controls.

Syngenta's discussion of recovery may be limited to short-term exposures to atrazine in lotic habitats. Following a 2-day exposure to 10 μg/L atrazine, Johnson (1986) reported recovery by Day 7. If plant growth has been affected for a long time, the function of photosynthesis may recover, but the differences measured in biomass do not reflect parity with controls (Cunningham *et al*., 1984; deNoyelles *et al*., 1982; Herman *et al*., 1986; Plumley and Davis, 1980). Also, plants will not recover if the exposure duration was sufficient to kill some plant species, as reported by Kettle *et al*. (1987).

p. 40. **Syngenta Comment**: Syngenta cited 2 studies, Brockway et al. (1994) and Benjamin (1996) as examples of rapid recovery following atrazine exposures.

EFED Response: In both cases, the authors tested phytoplankton species. Brockway *et al*. conducted a series of atrazine exposures on microcosms with 5 phytoplankton species over a period of 75 days. The exposures produced rapid reductions in oxygen production. A 5 μg/L exposure reduced oxygen production by 10%, 50 μg/L reduced it by about 33%, and 100 μg/L reduced it by 50 percent. Recoveries occurred in 1 or 2 days depending on the test concentration.

Syngenta did not provide a reference for the article by Benjamin (1996), which would allow EFED review. Also, Syngenta did not provide an example of recovery for aquatic vascular plants following prolonged exposure.

P. 41-42 **Olfactory Response and Endocrine Effects**

p. 41. **Syngenta Comment**: Syngenta commented on the preliminary status of the olfactory response which may affect homing of salmon to spawning streams. Syngenta also provided summaries of atrazine concentrations reported from NAWQA study units in the Pacific west and New England where salmon enter fresh waters.

EFED Response: The Agency is concerned about the possible effect of atrazine and other pesticides on the homing ability of salmon. Additional research is needed to validate the pesticide effects on salmon before a risk assessment and any regulatory decisions can be made.

p. 42. **Syngenta Comment**: Syngenta indicated that the current EFED risk assessment did not focus on endocrine effects in wildlife species. Syngenta submitted three wildlife studies, a risk-based assessment addressing endocrine effects on wildlife species, and a 6(a)(2) submission on atrazine effects on the African-clawed frog (*Xenopus laevis*).

EFED Response: EFED has reviewed the four documents. The results of alligator and turtle egg studies on atrazine effects indicated no adverse effect on the sex in the eggs exposed to temperatures favoring development of males when exposed to 0, surfactant, 10, 50, 100, and 500 μg/L for 10 days. At hatch, egg fluids were analyzed for atrazine levels. The analyses indicated that atrazine levels in the egg fluids were below the detection limit (of< 20 μg/L wet weight). These analyses of egg fluids suggest that atrazine did not penetrate the egg shell and/or shell membrane.

In the *Daphnia pulicaria* study, the females did not yield males at any atrazine level (i.e., 0, 0.93, 4.1, 8.7, 44, 87 μg/L). This study indicates that atrazine does not produce endocrine effects in offspring of female *Daphnia pulicaria* exposed to likely atrazine concentrations for up to 12-days.

Three replicates of thirty, 4-day old African clawed frog tadpoles (*Xenopus laevis*) were exposed to each treatment at nominal concentrations of 0.01, 0.1, 1.0, 10.0 and 25 parts per billion (ppb) through metamorphosis (Hayes *et al*. in press). Atrazine exposures had no effect on mortality, time to metamorphosis, length or weight at metamorphosis. Up to 20 percent (16 to 20%) of the male frogs exposed to $\geq$ 0.1 ppb atrazine had gonadal abnormalities including multiple testes and/or ovaries (no gonadal abnormalities occurred in controls).

Hayes *et al*. conducted a second experiment with atrazine tested nominal atrazine concentrations of 0.1, 0.4, 0.8, 1.0, 25 and 200 ppb. Atrazine concentrations were confirmed in both experiments. Control males had larger larynges than females at metamorphosis. In both studies, treated males had a threshold effect on reducing laryngeal diameters (demasculinized) at $\geq$ 1.0 ppb compared to controls. Kendall's rank coefficient suggested a dose effect with increasing atrazine concentrations ($p < 0.01$). Adult male and female *Xenopus* exposed to 25 ppb atrazine for 46 days suffered a 10-fold decrease in plasma testosterone. No raw data were available for statistical analyses.

Syngenta in an oral presentation to OPP provided the results from atrazine tests on the African clawed frog. There were no effects on the sex ratio of frogs exposed to atrazine concentrations of 0.01, 0.1, 1.0, 10 and 25 ppb during critical phases of development (undefined periods). The results of their study were reported as follows. "The ethanol solvent control exhibited significant activity on the frogs including effects on mortality, length, and development time. The possible confounding effect of ethanol within all treatments including atrazine is not known. There was no convincing evidence that atrazine increased the larynx cross-section area, although statistically significant differences were noted, especially in the 25 ppb group, and at high doses in various *ad hoc* tests performed. Unequal group sizes and other potential confounding study design elements further complicate interpretation. In addition, variability in the time course of frog ontogeny and potential tank effects, coupled with the lack of an 'estrogen' positive control group, prevented clear conclusions to be drawn from this preliminary study. Additional statistical analyses and studies are planned to further investigate these questions."

The information on the Syngenta study did not provide any raw data. It is obvious that the level of ethanol was too high because it caused mortality and growth effects. The ethanol concentration was not reported and the number of mortalities were not reported. When the solvent controls demonstrate effects, the results of the study are compromised and the study is invalid.

Atrazine effects on tadpoles are a concern, because atrazine use coincides with spring rains and the breeding season for amphibians. While these gonadal abnormalities and laryngeal alterations raise concerns about adverse effects on amphibian reproduction, there is no conclusive evidence that these changes have an adverse effect on amphibian reproduction. Additional testing with atrazine-treaded tadpoles and adult frogs should be conducted to determine what, if any, effects occur on reproduction.

In a recent study submitted by Syngenta, largemouth bass were exposed to nominal concentrations of technical grade atrazine (purity 97.1%) at 0, 25, 35, 50, 75, and 100 µg/L. Additionally, bass were exposed to commercial grade (purity 42.1%) atrazine at 100 µg/L. After 20 days, plasma concentrations of estradiol, 11-ketotestosterone, testosterone, and vitellogenin (a protein that serves in yolk formation) were measured.

Although the study concluded that atrazine treatment did not affect plasma steroid or vitellogenin levels, EFED believes that the study is confounded by the high level of variability in the test results. Results do show, however, that in spite of high levels of variability atrazine treatment significantly increased plasma estradiol in females and significantly decreased plasma 11-ketotestosterone in males. Although not statistically significant, vitellogenin levels in atrazine-treated female fish appeared to be elevated relative to controls. Additionally, the presence of quantitative levels of plasma vitellogenin in male bass is of particular concern since the protein is normally only expressed in females; males can be induced to synthesize vitellogenin if exposed to an estrogenic compound. Furthermore, the formulated endproduct appeared to have enhanced effects on plasma steroids and vitellogenin levels relative to technical grade atrazine

The Endocrine Disruptor Screening Program has proposed a number of test protocols for identifying endocrine effects in wildlife species. Some of these protocols are currently in round-robin testing. As of this date, none have been approved for regulatory testing.

p. 43-45 **Syngenta Comments on NAWQA Data:** Syngenta questions EPA's use and interpretation of the NAWQA data, particularly the RED chapter's statement that "It is important to note that the NAWQA monitoring data were not specifically designed to time monitoring to correspond to Atrazine applications or specifically oriented to Atrazine treatment areas. Thus they are likely to underestimate the concentrations likely to be present in streams."

EFED Response

EFED agrees with Syngenta's attempts to use as full a dataset as possible for the NAWQA data, but continues to note relevant qualifiers on the sampling plan(s) and thus the appropriate inferences that can be drawn from the data. Because of these and the different types of waterbodies monitored, there is good reason to analyze the data by type of monitoring. In recent correspondence with EFED, USGS staff explained that some NAWQA sites were more heavily selected "toward atrazine use/runoff period in high use areas (i.e., IN, OH, IL, etc.) just as we weighted sampling to other high use chemicals in other areas (i.e., dormant sprays in December in California, pre-emergence in lawns in SE in Jan./Feb that coincide with wet season/runoff)..." There was agreement with EFED's statement concerning the potential for underestimation, "[The] Real issue is whether we captured the true peak. Probably not..." estimating that perhaps the 95th%ile values were captured, and concluding that "[the chapter] statement regarding 'underestimat[ing] the peak,' last sentence [is] true." (Personal correspondence with David Wangsness, USGS)

With regard to the use of 40 agricultural indicator sites, at the time of our analysis, these sites represented all available NAWQA agricultural indicator sites. Some indicator sites may be associated with high atrazine uses whereas others may not have any atrazine use. EFED did consider all the available data for the assessment, and presented the results in different ways. The table on page 32 (of the RED chapter) considered all available monitoring data and derived the exceedence probabilities from all values, whereas Figure 11 (on page 34) was constructed based on the monitoring peak for each agricultural indicator site.

In Syngenta's detailed review, they should provide the results for all indicator (agricultural or urban) or integrator sites with a similar approach, rather than considering all data in a single analysis.

p. 49 and 52 **Syngenta Comments on Trend Analysis:** Syngenta has submitted summaries of monitoring data and trend analysis from Lake Erie tributary drainage basins, from reservoirs supplying certain CWS's in the midwest, and from surface and groundwater sources in the state of Iowa, to support the contention that atrazine levels are declining in these areas and elsewhere.

EFED Response

Without a detailed review of the sampling designs and individual raw data from these many studies, EFED can not provide a definitive assessment. In general, however, EFED agrees that levels appear to be declining over the years in many of the streams and reservoirs sampled. Continued sampling programs are necessary, however, to monitor levels representative of both the longer term concentrations as well as those representing the highest peaks. While upper percentile levels reported in some years are often lower than those reported in other years, there appear to be many peaks each year representing very high concentrations. In addition, there are still numerous reports of MCL exceedences in both raw and finished water, with highest values indicating that in many areas there may still be concerns.

p. 50 **Syngenta Comments on Estuary Monitoring Data**: Syngenta asks for references for the data presented in the chapter, and presents Chesapeake Bay data that are lower.

EFED Response

The data used to generate the table on p. 38 of the draft RED were based on USDA results. The reference was included in Appendix VIII, with the web address: www.agnic.nal.usda.gov/cbp/pest/atrazine.html). There are a total of 106 surface water (SW) data sets based on station-year. The statistics in this table were generated by plotting the maximum value of each study-year based on the Weibull plot, using 105 study-years, and without including the highest value of 1662.50 ppb, reported for Study ID: 94022, Site: Owl Run, Station: TF-2X in 1988. The correct statistics should be 10.3, 2.7, 1.2 and 0.4 ug/L (ppb) for 95th percentile, 90th percentile, 75th percentile, and 50th percentile, respectively. These values have been changed in the RED. The correct values have been reported in Appendix VIII. The data set included several studies and several years (from 1976 to 1992).

With regard to the report(s) mentioned by Syngenta, it is possible that the observed values can be lower, just as they may turn out to be higher than those reported. The reported values were based on monitoring results, and obviously, if the high values were not caught then the high values were not being reported. Since the design of the monitoring study is very important, without details on the design, EFED derived the results based on maximum values of 105 station-years to construct the exceedence plot and statistics (as shown in the plot and table).

EFED agrees that a more comprehensive database for both the Chesapeake Bay and the Terrebonne Watershed would present a much more complete risk characterization for each over both time and space. The data reported, however, demonstrate the atrazine levels that have been and can be reached in these two examples of estuarine (and freshwater) environments. The Terrebonne Watershed covers an area extending from the Mississippi River on the north to the Gulf of Mexico to the south. The topography of the entire basin is lowland and all of the land is subject to flooding except the natural levees along major waterways. The coastal portion of the basin is prone to tidal flooding and consists of marshes ranging from fresh to saline.

p.51-57 **Syngenta Monitoring Data–PLEX/VMP and Rural Well Survey:** Syngenta reports <30% positive values in surface water or blended sources over the years 1993-99, and a very low percentage of detect's in groundwater CWSs (<3%). They also report only 4 systems with period means greater than the MCL for that 7-year period.

EFED Response

Because the OPP human health endpoint is postulated to occur after a relatively short (seasonal) length of exposure, drinking water levels must be examined for durations of this length. The "period" mean that Syngenta refers to is presumably a mean for the **7-year period** of study. When data for such an extended period as this are combined, most high peak exposures are expected to be "averaged out" in the presentation.

Furthermore, the most recent 6(a)2 report received from Syngenta by EFED on December 7, 2001 showed two hundred twenty-one (221) incidents during one month of June, 2001, with atrazine detections exceeding 3.0 ppb. The reports came from Illinois, Kansas, Indiana, Iowa, Kentucky, Ohio, Missouri, and Louisiana Among these 221 detects, 45 were for finished tap water, with a highest value of 12 ppb.

p. 52 to 56: **Syngenta Comments on Rural Well Survey**–Resampling of 14 high wells of an original sample of 1,505 rural wells showed lower values, with all atrazine levels <MCL and all 14 TCT levels under the DWLOC of 12.5 ppb. Syngenta claims point source contamination for the original wells with high values and also cites karst conditions at these.

<u>EFED Response</u>

One issue regarding the design of the rural well survey that EFED has pointed out previously is that only one sample was taken for each well. In earlier EFED comments and in discussions with SRRD, HED staff, and Syngenta, this issue was identified based on analyses of the ARP groundwater database. The ARP data have shown significant monthly variations, which clearly demonstrate that only one low detection value for a well can not rule out the possibility of higher values at different times. For this reason, it would be interesting to examine any resampling data Syngenta might have from other wells in the original survey, even if their original result was less than the MCL at the time.

Syngenta claims there is more spatial variation in the data than the temporal variation obvious in the ARP study. This may not always be the case, depending on the spatial and temporal sampling intervals in any given study. OPP would be interested in seeing Syngenta's data and analysis of the NAWQA studies regarding this issue. While it can be a matter of discussion as to which variability is greater in general, it is clear that both contribute to the uncertainty of the estimates, and the best sampling design would take into account some aspects of both spatial and temporal variability. The fact of only one sample per well for the RWS continues to contribute heavily to the uncertainty of any estimates made from these data.

In addition, the original Rural Well Survey was a sample of private rural wells, albeit one that was originally skewed for the purpose of providing an upper estimate of exposure. As a sample of wells, it represents a larger population of rural wells that serves a larger population of people. Syngenta should present the population(s) of people exposed to drinking water from private rural wells as part of its discussion.

p. 57-58 and 65-74 Modeling Input Parameters, Fate and Exposure Characterization

Syngenta has questioned EFED's use of environmental fate data for the model inputs in PRZM/EXAMS simulations. Syngenta commented that more environmental fate data are available and that EFED should not base the assessment solely on the submitted studies. EFED is finalizing its reviews of submitted studies and stands by its initial choice of data. However, to determine whether Syngenta's suggested inputs made any difference in the outputs, EFED re-ran PRZM/EXAMS **based on Syngenta's suggested inputs** to see the impact on the exposure results. The results are tabulated below.

There are three scenarios. The first one is based on the original values used in the RED, and the second and third scenarios are based on Syngenta's suggested environmental fate inputs. In the original modeling runs for the RED, EFED assumed the values of 75% application efficiency and 5% off-target spray drift for aerial applications. These assumptions are not as conservative as some of the Spray Drift Task Force (SDTF) results indicate. For example, the value of off-target spray drift can be up to 15%. According to the current EFED guidance on modeling inputs, for aerial applications, the application efficiency should be 95% and the off-target spray drift should be 5%. For ground applications, the values are 99% and 1%, respectively.

Scenarios 2 and 3 represent the results of different application efficiency values of 75% and 95%, respectively. In addition, Syngenta has claimed that ground applications are the common practice for sugarcane use in Louisiana. For this reason, EFED also ran the ground application of 99% efficiency and 1% off-target spray drift for sugarcane use with Syngenta's suggested input values. The results are in scenario 4. Comparing the results of different scenarios for each use, the differences are not significant. This is true even when the drift value is fixed at 5%, compared with the default drift value of SDTF's AgDRIFT model of 15%.

Treated Crop	Scenario	Atrazine EEC Values ppb (μg/L)				
		Peak Conc.	96-hour Average	21-day Average	60-day Average	90-day Average
Sugarcane (4.0 lb ai/a)	1	205	204	202	198	194
	2	167.6	166.7	163.8	157.8	152.9
	3	207	206	203	195	189
	4	200.6	199.6	196.7	189.8	183.8
Corn (2.0 lb ai/a)	1	38.2	38.0	37.2	35.5	34.2
	2	29.7	29.4	28.4	26.6	25.1
	3	35.3	35.0	33.8	31.6	30.0
Sorghum (2.0 lb ai/a)	1	72.7	72.3	70.6	67.7	65.9
	2	47.9	47.4	46.0	42.7	40.4
	3	58.4	57.8	56.0	52.0	49.2