~~May 2, 2003~~May 5, 2003

Public Information and Records Integrity Branch
Information Resources and Services Division (7502C),
Office of Pesticide Programs
Environmental Protection Agency,
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460-0001
Submitted by Email to opp-docket@epa.gov

Attn: Docket # OPP-2003-0072
Atrazine IRED, 68 Fed. Reg. 9652 (Feb. 28, 2003)

On behalf of the Natural Resources Defense Council (NRDC), we submit these comments on the Environmental Protection Agency's (EPA) Interim Reregistration Eligibility Decision (IRED) for Atrazine (Jan. 31, 2003). These comments supplement our prior filings regarding this chemical, and our prior comments on the atrazine human health and ecological risk assessments. NRDC reiterates its previous comments urging EPA to cancel atrazine's registration and revoke all atrazine tolerances.

NRDC uses law, science, and the support of more than 500,000 members nationwide to protect the planet's wildlife and wild places and to ensure a safe and healthy environment for all living things. NRDC has no direct or indirect financial or fiduciary interest in the manufacture or sale of atrazine or any other pesticide or chemical.

SUMMARY
The following concerns are discussed in detail in these comments:

I. The atrazine IRED inappropriately permits excessively high drinking water contamination, drinking water clean-up costs are passed to the consumer, and wildlife is unprotected.

II. EPA has violated its special review regulations, FIFRA, the Federal Advisory Committee Act, the Administrative Procedure Act, and the Agency's September 1984 settlement with NRDC, by meeting repeatedly and privately with atrazine's registrant and cutting a special private deal with the registrant that is contrary to the public interest.

III. EPA's atrazine decision allows and even encourages violations of the safe drinking water act (SDWA), and thus contravenes the FFDCA and FIFRA as well.

IV. EPA's NOAEL is unjustified because it is a level at which adverse effects were observed. Moreover, Congress required EPA to regulate based on NOELs not NOAELs.

V. Agriculture and lawn care risks are unacceptably high, and EPA's proposed mitigation is insufficient.

VI. Ecological risks are unacceptably high, and no effective mitigation is proposed.

VII. The ongoing registration of atrazine jeopardizes endangered species and their critical habitat.

VIII. Atrazine has been associated with an increased risk of cancer in several studies.

IX. Substantial data demonstrate that atrazine is an endocrine disruptor.

X. Conclusion.

DETAILED COMMENTS

I. THE ATRAZINE IRED INAPPROPRIATELY PERMITS EXCESSIVELY HIGH DRINKING WATER CONTAMINATION. DRINKING WATER CLEAN-UP COSTS ARE PASSED TO THE CONSUMER. WILDLIFE IS UNPROTECTED

Most dietary atrazine exposure occurs through drinking water, with almost none from food. Therefore, the drinking water level of comparison (DWLOC) represents essentially the amount of atrazine that EPA believes is safe to consume. When model or monitoring data exceed the atrazine DWLOC, then EPA states that it has exceeded the Agency's level of concern (LOC). The Agency had determined that the DWLOC for infants, the most vulnerable population subgroup, was 12.5 ppb, based on a NOAEL of 1.8 mg/kg/day (six-month LH surge in a rat) and a 1000X UF (10X inter, 10X intra, 10X FQPA for uncertainties associated with atrazine's toxic effects on the developing child and the extent and magnitude of exposure to atrazine in drinking water). EPA suggests that the increased monitoring program could allow the removal of that portion of the 10X FQPA associated with exposure uncertainties, thereby reducing the 10X to 3X for any risk assessments conducted in monitored areas. Therefore, in the IRED, the new DWLOC is re-calculated to be 37.5 ppb, based on an endpoint of 1.8 with a 300X UF (10X inter, 10X intra, 3X FQPA for uncertainty associated with atrazine's toxic effects on the developing child) (IRED, p. 84).

The intermediate-chronic DWLOC for infants is 12.5 ppb (seasonal average) for unmonitored areas, and 37.5 ppb for monitored areas. There are 37 community water systems (CWS) that exceed 12.5 ppb, the Agency's level of concern at the 99.9th exposure percentile for infants, children 1-6 yrs, and adults, according to the manufacturer's monitoring data. The acute dietary drinking water risks, and chronic food risks are below the EPA's LOC.

EPA states in the IRED that "if an exceedence of 37.5 is detected in raw drinking water (pre-treatment) in any of these watersheds, further use of atrazine will be prohibited in that watershed" (IRED, p. 84). Unfortunately, this level is far from protective for two reasons: first, adverse effects in aquatic plants and animals have been reported at levels of 10 ppb, and in some studies at levels as low as 0.1 ppb; second, the level of 37.5 ppb is

a seasonal average that would allow peak levels far in excess of this level during the spring – the key time for reproduction of aquatic plants and animals.

Furthermore, exposure through domestic wells exceeds the level of concern. Eight wells out of 1505 wells monitored in high atrazine use areas had residues greater than 12.5 ppb. Approximately ten percent of the US population gets their drinking water from 13 million wells, therefore the sample taken is highly inadequate. Thus, EPA has completely ignored the known aggregate risks of atrazine contamination to private well owners (and users of springs and other non-regulated water systems), in direct violation of the aggregate risk requirements of FFDCA § 408(b).

II. EPA HAS VIOLATED ITS SPECIAL REVIEW REGULATIONS, FIFRA, THE FEDERAL ADVISORY COMMITTEE ACT, THE ADMINISTRATIVE PROCEDURE ACT, AND THE AGENCY'S SEPTEMBER 1984 SETTLEMENT WITH NRDC, BY MEETING REPEATEDLY AND PRIVATELY WITH ATRAZINE'S REGISTRANT AND CUTTING A SPECIAL PRIVATE DEAL WITH THE REGISTRANT THAT IS CONTRARY TO THE PUBLIC INTEREST.

The IRED reflects a private deal between atrazine's registrant Syngenta and the agency. The agency apparently met repeatedly with the registrant in hammering out a deal, and based upon our review of the docket all or virtually all of these meetings apparently were not fully and timely summarized and docketed as legally required. In reaching this private deal, EPA has clearly failed to follow the letter and spirit of its Special Review regulations governing public and transparent decision-making on pesticides such as atrazine that are in Special Review. *See* 40 C.F.R. Part 154. For example, EPA's regulations require that the agency fully and timely docket "all comments, correspondence, or other materials" submitted by registrants and other outside parties regarding atrazine, "all documents, proposals, or other materials concerning" atrazine provided by EPA to outside parties, and summaries of all meetings with the registrants or other oputside parties. *Id.* §§ 154.15(b)(7)-(9); 154.27(c). The memo summarizing the meetings with registrants and outside parties "shall be placed in the docket within 10 working days of the subject meeting," and the materials from outside parties or provided by EPA to outside parties must be docketed within 15 working days. *Id.* 154.15(d). The docket index must reference all such documents and be publicly disseminated. *Id.* 154.15(f). In addition, the rules provide that while meetings with private parties are not prohibited, "during such meetings, the Agency *will not commit to take any particular action concerning a pending decision*." *Id.* § 154.27(b)(emphasis added). Moreover, the final decision is not to be a result of a private deal cut with the registrant; the rules explicitly mandate that "the Agency will make the final administrative decision *on a wholly independent basis* and in accordance with the law." *Id.* § 154.27(b)(emphasis added).

Contrary to EPA's rules, it appears that the agency met with Syngenta frequently without adequate and timely docketing, and that the agency reached a private deal with Syngenta. Specifically, the agency announced in its January 31, 2003 Press Release that "The

provisions of this action, contained in the IRED, have also been incorporated into an agreement with the principal registrant of atrazine, Syngenta." Obviously, as is evidenced by the Press Release and the written agreement with Syngenta, EPA *did* "commit to take [a] particular action concerning a pending decision" in consultation only with Syngenta, in direct violation of its regulations.

Not only does this process of private deal making violate EPA's Special Review rules at 40 C.F.R. Part 154, it also violates the Federal Insecticide, Fungicide, Rodenticide and Rodenticide Act (FIFRA), 7 U.S.C. §136 *et seq.*, the Federal Advisory Committee Act (FACA), 5 U.S.C. App. II, and the Administrative Procedure Act (APA), 5 U.S.C. §551 *et seq.* (APA). As NRDC alleged in detail in its complaint in *NRDC et al. v. EPA*, Civ. Action No. 83-1509 (D.D.C., filed May 26, 1983), EPA simply cannot meet repeatedly with registrants (in this case Syngenta) or other industry representatives to reach an agreement on an important public policy and public health issue such as how to regulate atrazine.

FIFRA and EPA rules require that EPA act independently in carrying out its mandate to protect public health and the environment. Congress expressed its intention under FIFRA to prohibit such private or closed negotiations or protracted and secret discussions of risks and benefits between the industry and EPA.

FACA requires that if EPA establishes a group of outside advisors on an issue, or utilizes advice from outside parties, it may do so only in compliance with FACA. To establish or utilize such advice, EPA must establish a balanced advisory committee that meets in the open and in accordance with all FACA procedural requirements, is "fairly balanced," and is not "inappropriately influenced…by any special interest." 5 U.S.C. App. II. EPA obviously solicited and in an ongoing fashion utilized the advice of Syngenta on what regulatory actions would be appropriate to deal with atrazine, yet the agency failed to comply with any of FACA's procedural and substantive requirements, in direct violation of the Act.

Moreover, the APA requires that in making regulatory decisions, EPA may not give preferential access to any one side of the debate, and may not cut private deals with a regulated industry. The agency may not issue a rule that has been negotiated with only one party, and then provide what amounts to an empty opportunity for public comment.

Finally, EPA entered into a consent agreement with NRDC on September 20, 1984 in which the agency agreed to open up its pesticide review process. EPA agreed to, *inter alia*: use a comprehensive public docketing system; docket minutes of all meetings with persons outside of the government; prohibitions against providing draft decisions or other documents solely to industry representatives; procedures to assure that EPA independently makes all decisions with docket summaries of meetings; and to refuse to make private deals with registrants. *See* NRDC Motion to Dismiss NRDC v. EPA, Civ. Action No. 83-1509 (D.D.C., Motion filed January 24, 1986), (attached). Many of these requirements were embodied in EPA regulations noted above. It is profoundly troubling that history seems to be repeating itself, and that EPA appears to be reverting to cutting

private deals after private negotiations with registrants. We note that EPA agreed that if the agreed procedures were not followed for a chemical, that NRDC has a right to move the Court to enforce the agreement with respect to such pesticides.

The clear evidence that EPA has shunted aside legal restrictions on its decision-making procedures would be somewhat less troubling if the Agency had reached a decision that fully protected public health and the environment. However, by mandating nothing more than additional monitoring and setting a "trigger level" at 37.5 ppb, which is over 12 times the 3 ppb MCL for atrazine, EPA has effectively punted the cost of clean-up to the water utilities, and eventually to the consumer. We believe that this is a bad policy and is unfair. The EPA decision also leaves essentially helpless hundreds of thousands or millions of people who use groundwater-supplied systems that will not be required to have their source water monitored, who use private wells, or who use smaller public or private water systems in areas with high atrazine use that are unaware of atrazine problems and have not installed treatment. Moreover, it leaves environmental harms unaddressed. Aquatic wildlife remains unprotected.

III. EPA'S ATRAZINE DECISION ALLOWS AND EVEN ENCOURAGES VIOLATIONS OF THE SAFE DRINKING WATER ACT (SDWA), AND THUS THE FFDCA AND FIFRA AS WELL.

The current EPA drinking water standard (Maximum Contaminant Level, or MCL) for atrazine, codified in the C.F.R., is 3 ppb (annual average of 4 quarterly samples). *See* 40 C.F.R. §141.62(c). Moreover, EPA has determined, through notice and comment rulemaking, that the MCL Goal (MCLG) – the "level at which no known or anticipated adverse effects on the health of persons occur, and which allows an adequate margin of safety" – for atrazine is 3 ppb, a level also codified in the C.F.R. *See* 40 C.F.R. §141.50(b).

Yet EPA's private deal with Syngenta states that *no action will be required* unless water used by a public water system exceeds 37.5 ppb, a concentration over 12 times higher than EPA's duly-promulgated tap water standard. It is impossible, if any tap water sample exceeds even 12 ppb, for a public water system to be in compliance with the MCL. Thus, EPA's private deal effectively allows or even encourages widespread, unabated contamination of the source waters used by potentially millions of Americans for drinking water with atrazine at levels that violate the agency's own tap water standard. This is despite the Agency's formal determination, through a notice and comment rulemaking that has not been repealed, that the promulgated MCL is the highest level at which there will be no known or anticipated adverse effects on the health of persons. EPA is not free to ignore the agency's own duly-promulgated drinking water safety standard and MCLG for atrazine, and therefore cannot lawfully find under the FFDCA that it is "safe" for drinking water to contain atrazine at a level in excess of 3 ppb.

In a strange twist, under EPA's currently enforceable rules, any public water system with over 3 ppb atrazine in its water must issue to all of its customers the following notice:

> The United States Environmental Protection Agency (EPA) sets drinking water standards and has determined that atrazine is a health concern at certain levels of exposure. This organic chemical is a herbicide. When soil and climatic conditions are favorable, atrazine may get into drinking water by runoff into surface water or by leaching into ground water. This chemical has been shown to affect offspring of rats and the heart of dogs. EPA has set the drinking water standard for atrazine at 0.003 parts per million (ppm) to protect against the risk of these adverse health effects. *Drinking water that meets the [3 ppb] EPA standard* is associated with little to none of this risk and *is considered safe* with respect to atrazine.

40 C.F.R. §141.32(28)(emphasis added). It is unfathomable how EPA can take directly conflicting positions under the SDWA and the FFDCA/FIFRA. Under the SDWA, EPA has promulgated rules setting an enforceable MCL of 3 ppb, providing that the 3 ppb MCLG is the highest safe level in drinking water, and explicitly ordering any water utility serving drinking water at over 3 ppb to warn their customers that they are getting drinking water containing more than the "safe" level of 3 ppb. Yet on the other hand the agency's pesticide program now says that it is perfectly "safe" under the FFDCA and FIFRA for Syngenta to continue to sell atrazine and for it to contaminate drinking water at up to 37.5 ppb. This is arbitrary and capricious decision-making at its most clear.

While the SDWA MCL applies to public water systems, not to Syngenta *qua* registrant of atrazine, the agency's private deal with Syngenta not only encourages violations of the EPA atrazine MCL in a manner contrary to public policy and Congressional intent, it directly violates the SDWA, FIFRA, and the FFDCA. Under the latter two statutes, the agency may not authorize contamination of water used for drinking in excess of its drinking water standard. FIFRA provides that EPA may not register a pesticide unless, "when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment." FIFRA §3(c)(5)(D). Moreover, FIFRA §2(bb), 7 U.S.C. §136(bb), provides in defining "unreasonable adverse effects on the environment" that there shall be no "human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under" FFDCA §408, 21 U.S.C. §346a. The term "food" includes drinking water. 21 U.S.C. §321(f). Under the FFDCA, EPA must determine that all aggregate exposure to atrazine, including all exposure to atrazine in drinking water, is "safe," meaning that there is a "reasonable certainty of no harm" to any person, including infants, children, and other vulnerable populations. EPA simply cannot determine that exposure to atrazine at a level of over 12 times its duly-promulgated drinking water standard is "safe" and that there is a "reasonable certainty of no harm" from that exposure.

EPA's decision also contravenes the Safe Drinking Water Act, because the agency is authorizing and indeed encouraging drinking water contamination up to 12 times the atrazine MCL, effectively a back-door relaxation of the SDWA health standard in violation of the SDWA. EPA is prohibited from adopting a weaker atrazine MCL under the anti-backsliding provision of the SDWA §1412(b)(9), 42 U.S.C. §300g-1(b)(9). As

was recently reiterated by the U.S. Court of Appeals for the D.C. Circuit in a decision involving the radionuclides MCLs, *City of Waukesha v. EPA*, No. 01-1028, slip op. at 21, 47 (Feb. 25, 2003), and as EPA acknowledged in briefing that case, the agency is prohibited from weakening MCLs for contaminants under the anti-backsliding provision. Even if EPA were not prohibited by the SDWA anti-backsliding provision from weakening the atrazine MCL, the agency clearly could not effectively weaken that standard without going through the full SDWA §1412, 42 U.S.C. §300g-1 process, including notice and comment rulemaking and a full scientific and other analysis as mandated by that Act. EPA has done none of this analysis. Therefore, EPA's private deal also contravenes the SDWA.

IV. EPA'S NOAEL IS UNJUSTIFIED BECAUSE IT IS A LEVEL AT WHICH ADVERSE EFFECTS WERE OBSERVED. MOREOVER, CONGRESS MANDATED THAT EPA MUST USE THE NOEL, NOT A NOAEL.

EPA has used a six month study in Sprague-Dawley (SD) rats to determine a No Observable Adverse Effect Level (NOAEL), based on leutinizing hormone (LH) surge attenuation (MRID44152102). In this study, EPA determined that atrazine had adverse effects at 3.65 mg/kg/day (based on estrous cycle alterations and LH surge attenuation), and treated this dose as its lowest observed adverse effect level (LOAEL). Accordingly, the Agency chose the next lowest dose tested, 1.8 mg/kg/day, as its NOAEL.

There are numerous legal and scientific problems with EPA's approach. First, Congress ordered the agency to set tolerances at a "safe" level at which there is a "reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue . . ." FFDCA §408(c)(2). Congress made it clear in the Legislative History that it expected the tolerance to be based not upon a LOAEL or even a NOAEL, but based upon a No Observable Effect Level (NOEL). As the House Report states:

> In the case of a threshold effect for a pesticide chemical residue, the Committee expects that a tolerance will provide a "reasonably certainty of no harm" if the Administrator determines that the aggregate exposure to the pesticide chemical residue will be lower by an ample margin of safety than the level at which the pesticide chemical residue will not cause or contribute to any known or anticipated harm to human health. The Committee further expects, based on discussions with the Environmental Protection Agency, that the Administrator will interpret an ample margin of safety to be a 100-fold safety factor applied to the *scientifically determined ''no observable effect'' level* when data are extrapolated from animal studies.

H.R. Rep. No. 104-669 part 2 at 41 (July 23, 1996) (emphasis added). Thus, EPA must use the NOEL, not a LOAEL or NOAEL as it has here for atrazine.

Moreover, even assuming that it were lawful to use a NOAEL instead of a NOEL, EPA's NOAEL determination is seriously flawed on scientific grounds. The agency relies on what it says is a NOAEL as the most sensitive toxicity endpoint for its chronic and

intermediate-term health assessment. NRDC raised concerns that there were treatment related effects at the lowest dose tested (NRDC comments July, 2002). EPA summarized NRDC's comments and presented the Agency's response as follows:

> Comment: NRDC believes that 1.8 mg/kg bw per day is the lowest observed adverse effect level (LOAEL) rather than the no observed adverse effect level (NOAEL) for suppression of the LH surge in the 6 month LH study and its NOAEL.
> HED Response: EPA's position is that 1.8 mg/kg bw per day is a NOAEL in the 6 month LH surge study by Syngenta. EPA believes it is justified in using 3.6 mg/kg bw per day as a LOAEL for this endpoint. The rationale for the selection of 3.6 mg/kg bw per day as a LOAEL and 1.8 mg/kg bw per day as a NOAEL for suppression of the LH surge is based on a weight of evidence argument. There is a dose response trend for suppression of the LH surge. While the 3.6 mg/kg bw per day dose does not represent a statistically significant decrease in the amount of LH, the dose response trend is supported by the statistically significant difference in vaginal cycling at 3.6 mg/kg bw per day. Vaginal cycling data tends to be less variable than LH data. Thus, EPA acknowledges that selection of 1.8 mg/kg bw per day as a NOAEL for LH suppression is conservative, but errs on the side of health protection. Although there is one statistically significant response for suppression of the LH surge in the 1.8 mg/kg bw per day dose group for one time point, this is not sufficient evidence to designate 1.8 mg/kg bw per day as a LOAEL, particularly in light of the fact there were no statistically significant differences found for vaginal cycling at this dose.[1]

Although EPA acknowledges that the lowest dose tested, 1.8, did have one statistically significant response for suppression of the LH surge, the endpoint of interest, it maintains that vaginal cycling (number of days in estrus) was not significantly affected at this dose. However, while the study design was flawed and underpowered, so that even large treatment effects are not statistically significant, a dose-dependent trend is evident from the data, presented in the Table below.

TABLE 1: Six month study of atrazine: LH surge in SD rats (MRID 44152102). Summary data for each relevant toxicity endpoint, at each dose of atrazine is shown. All data is exactly as presented in the EPA data evaluation report. An asterisk represents EPA determination of statistical significance.[2]

Effect	**Control**	**Low dose 1.8 mg/kg/day**	**Med dose 3.65 mg/kg/day**	**High dose 29.44 mg/kg/day**
Increase in mean % days in estrus at week 21-22	Avg=32% SD=25%	Avg=41% SD=32%	Avg=45% * SD=32%	Avg=51% * SD=35%
Number of animals with estrus blocks, at week 21-22	21	31	38	50
Group mean LH values in repeat bleed animals At 1800 At 2000	 +267% +273%	 +237% +133%	 +157% +148%	 -15%* +4%*

It is clear from EPA data presented in the Table that atrazine adversely affects the LH surge, with expected effects on the estrus cycle, at all doses tested. The LH surge, even at the lowest dose of atrazine tested, is below the threshold critical for ovulation, as evidenced by concomitant increases in percent days in estrus and increases in the number of atrazine-treated animals with estrus blocks.

While the EPA dismisses the low-dose effects as not statistically significant, it is evident that the study design was underpowered, and unable to detect even large treatment effects. For example, none of the increases in the number of animals with estrus blocks are significant, at any dose, despite the evident dose-dependent increasing trend (21 v. 31, 38, 50). Further, the obvious dose-dependent increase in mean % days in estrus does not gain statistical significance primarily due to the large standard deviations, almost as large as the mean values themselves, even in the control group (mean=32%, SD=25%). This large variability in data is evidence of an underpowered study, with too few samples to detect even large treatment effects.

An examination of the data indicates that EPA has wrongly determined that the lowest dose tested is a NOAEL. Rather, there is a clear dose-dependent trend of all measured endpoints, at all doses tested. *It is incumbent on the agency to do a statistical test for trend across the doses.* If the EPA intends to use this study (MRID 44152102) to determine a no-effect level for atrazine exposure, then EPA has two possible choices: either EPA must use an uncertainty factor to extrapolate below the lowest dose tested, to estimate a no-effect level, or the Agency must do a benchmark analysis to identify the LED_{10} for these endpoints. It seems strange to us that the Agency did not do a benchmark analysis in this case, as it is our understanding that EPA has been moving toward incorporating this approach routinely in their non-cancer risk assessments. In either event, NRDC asserts that the EPA has no scientific justification for the claim that the lowest dose constitutes a no-effect level.

V. AGRICULTURE AND LAWN CARE RISKS ARE UNACCEPTABLY HIGH, AND EPA'S PROPOSED MITIGATION IS INSUFFICIENT.

Occupational agricultural exposure to atrazine exceeds the EPA level of concern. Workers who mix, load, and apply atrazine to agriculture, turf, and home lawns currently exceed the level of concern presuming baseline or label-stipulated personal protective equipment (PPE). The Agency has proposed to mitigate these risks with the following label changes: closed mixing and loading systems will be required for some aerial applications; maximum PPE (long shirts and pants, protective eyewear, dust/mist respirator) will be required for liquids and dry flowables; wettable powders will be packaged in water soluble bags for aerial and groundboom applications; closed cockpits will be required for aerial applications; closed cabs will be required for flaggers.

For occupational non-agricultural use, the following label changes will be made: baseline PPE (long shirts and pants, shoes and socks) will be required for granular formulations; baseline PPE plus gloves will be required for water dispersable granules and water soluble powders; maximum PPE will be required for liquid formulations; maximum single application rates for liquid formulations will be reduced from 2 to 1 lb ai/A; granular lawn products will be required to be watered in.

Residential uses of atrazine exceed the Agency's level of concern for some uses. Bellygrinder applications of granular formulations are of particularly great concern (MOE=65). The Agency proposes the following mitigation: hand-held devices used for granular formulations will be restricted to spot applications only; prohibit granular products for hand applications; reduce the maximum one-time application rate from 2 to 1 lb ai/A; require granular lawn products to be watered in. All homeowner handler assessments for residential applicator risks are done presuming short-sleeved shirts and short pants, considered a reasonable assumption by the EPA and NRDC.

Given the reality of poor compliance and limited enforcement of regulations and labeling, EPA's assumption of 100% compliance and enforcement leaves workers unprotected. There is poor compliance with EPA regulations and label restrictions, which include personal protective equipment, closed cab systems, lengthened re-entry intervals, and wash facilities.[3] [4] There is almost no enforcement of EPA regulations and label restrictions, making them practically ineffective. This is evident by approximately 2,000 pesticide poisoning incidents reported annually to the CDC, and to the EPA FIFRA 6(a)(2) system.[5] In light of evidence of poor compliance with EPA regulatory standards, the inaccurate assumption of full compliance will leave untold numbers of agricultural workers and residential users at unacceptably high risk, including some children, and some pregnant women.

VI. ECOLOGICAL RISKS ARE UNACCEPTABLY HIGH, AND NO EFFECTIVE MITIGATION IS PROPOSED.

In our comments on the Revised Preliminary Human Health Risk Assessment for atrazine, and our comments on the Preliminary Ecological Fates and Effects Risk Assessment (EFEC; November 2001) we urged EPA to take steps to cancel this dangerous pesticide. EPA itself concluded in 1996 that "[b]ecause of [atrazine and four other pesticides'] potential to contaminate ground water, EPA has determined that these pesticides may cause unreasonable adverse effects on the environment in the absence of effective management measures provided by" a State Management Plan (SMP). 61 Fed. Reg. 33,260 (June 26, 1996). EPA has not found that such SMPs have been effective at reducing atrazine levels below the drinking water standard, and any change in the agency's 1996 pronouncement and findings is an unsupported and unwarranted departure from the agency's previous well-documented findings. The Ecological Risk Assessment makes the case for cancellation far stronger, considering EPA's conclusion that:

> widespread environmental exposure has serious implications when compared to ecotoxicological endpoints of concern. The preliminary ecological risk assessment indicated that risk quotients exceeded the levels of concern for chronic effects on mammals, birds, fish, aquatic invertebrates and non-target plants are possible at maximum and in some cases typical use rates. A refined risk assessment focusing on the aquatic environment and using the extensive exposure monitoring data as well as additional ecotoxicological data found in the open literature, resulted in concerns for adverse toxicological effects on freshwater and estuarine plants and their communities as well as indirect adverse effects on aquatic invertebrate and fish populations at monitored atrazine levels in surface waters.[6]

The direct effects of atrazine on nontarget aquatic plants indicate a high risk, such that routine peaks in atrazine levels above 20 ppb cause death of some aquatic flora, and complete loss of some plant species (Reregistration Eligibility Science Chapter for Atrazine, Environmental Fate and Effects Chapter [EFEC], p. 60; Kettle et al, 1987[7]). As EPA acknowledges, these direct effects of atrazine alone may devastate the aquatic community by reducing oxygen levels and nutrients in the water, thereby risking further loss of aquatic plants and animals. EFED states that a reduction in primary production of algae (EC50=1 ppb), reduction in invertebrate populations (EC50=10 ppb), and a reduction in phytoplankton production (EC50=20 ppb) are real-world risks following seasonal atrazine exposures. The crippling effects on fish populations follow loss of aquatic vegetation within weeks to months (Atrazine EFEC at 21). Brook trout, among the most sensitive aquatic animal, has a chronic NOAEC value of 65 ppb, and fish populations are likely to suffer reductions due to food loss and habitat damage at 20 ppb[8]. At current use rates, atrazine may threaten the complex integrity of aquatic communities; a pond whose community is limited to only the most hardy, atrazine-resistant species may be less able to provide for the waterfowl and mammals who depend on aquatic environments for food and reproduction. EFED rightly agrees with Kettle et al, 1987, who maintain that at 20 µg/L, recovery is uncertain, species diversity is very important, and the combined effects of atrazine with other pesticides would lower the tolerance of the plants to atrazine toxicity, making the whole aquatic community more vulnerable. These authors found that a single application of 20 µg/L (ppb) of atrazine to a pond

reduced vegetation 60% within several months, and by 90% within a year. Bluegill (a very hardy species) was reduced 96% in a year. Indirect community effects resulted from the impacts of atrazine on aquatic vegetation (Atrazine EFEC at 21).

The Agency has concluded that atrazine is toxic to non-target plants (neighbor crops) at levels that exceed the Agency's level of concern. It is especially disturbing that the level of concern is exceeded from spray drift alone, or spray drift and runoff, even when assuming that spray drift is 5%, and runoff is 2%, both likely underestimates of actual drift and runoff.

The EFED report states that mammalian and avian reproduction chronic levels of concern (LOC) are routinely exceeded for several use scenarios (Atrazine EFEC at 64-66). Following maximum use rates on sugarcane, chronic LOC is exceeded for mammalian reproduction by as high as 90-fold (NOAEL is 50 ppm for adult body weight reduction, and 10 ppm for pup weight reduction), and 4-fold for avian species (NOAEL is 225 ppm for egg production). Typical use rates for sugarcane, corn, and sorghum all resulted in risk quotients which exceeded the LOC (Risk Quotient (RQ)=1) for mammalian and avian reproduction (RQ=26-62). These are extremely high RQ's, and clearly represent a hazard for wildlife populations.

In NRDC's view, the fact that risk quotients exceed EPA levels of concern for chronic effects on mammals, birds, and fish, as well as other organisms, for maximum and in some cases even typical atrazine use rates clearly suggests that the chemical is having adverse effects on the environment. Rather than an effective mitigation strategy, EPA is requiring the manufacturer, Syngenta, to perform more aggressive water monitoring. This passive strategy will, of course, have no effect on reducing atrazine levels. If an exceedence of 37.5 ppb seasonal average is detected in raw drinking water, then EPA writes that "further use of atrazine will be prohibited in that watershed" (IRED at 84). This strategy will allow continued use of atrazine in all watersheds, since no watershed currently exceeds the action-trigger of 37.5 ppb. Meanwhile, aquatic communities will continue to suffer population declines and adverse effects because it is clear that adverse effects occur at levels significantly below 37.5 ppb. NRDC believes that this is unacceptable. In view of the severe adverse environmental consequences detailed here and in our previous comments, and considering EPA's obligation under FIFRA to regulate pesticides in order to prevent "unreasonable adverse effects on the environment," FIFRA § 3(c)(5), we believe that atrazine can not safely be reregistered.

VII. THE ONGOING REGISTRATION OF ATRAZINE JEOPARDIZES ENDANGERED SPECIES AND THEIR CRITICAL HABITAT.

Based on EPA's IRED and ecological risk assessments, widespread environmental exposure to atrazine threatens endangered species throughout the country. Atrazine exposure exceeds EPA's LOCs for endangered terrestrial plants, aquatic plants, aquatic invertebrates, and fish, and may indirectly affect endangered birds, mammals, amphibians, reptiles, and beneficial insects. EPA has therefore acknowledged – but failed to take any steps to remedy – that atrazine may threaten hundreds of endangered species nationwide.

EPA acknowledges that atrazine is highly toxic, persistent, and mobile, and therefore poses significant threats to endangered species and other non-target organisms (IRED at 50-51). Atrazine is transported via spray drift and runoff to surface water, and it leaches into groundwater (IRED at 50). EPA notes that atrazine has been "widely detected" in air and rainfall samples in both high use areas and areas far removed from high use areas (IRED at 52). EPA has found that there is "widespread environmental exposure" to atrazine in aquatic communities and other ecosystems that may have many effects (IRED at 50). The laboratory, microcosm, mesocosm and field studies used by EPA "suggest that atrazine concentrations measured in the environment could reach levels that are likely to have negative impact on sensitive aquatic species and communities." (IRED at 61). The exposure of aquatic communities to atrazine at levels 10-20 ppb (significantly below the EPA proposed seasonal average level of concern of 37.5 ppb) can result in community-level and population-level effects (IRED at 4). In addition, atrazine exposure in aquatic communities may cause direct effects on aquatic non-vascular plants that could result in reductions in populations of aquatic macrophytes, invertebrates, and fish (Atrazine EFEC at 2). Atrazine indirectly affects aquatic communities through loss of species sensitive to atrazine and resulting changes in structure and functional characteristics of the affected communities. Because atrazine is used primarily during crop pre-planting and pre-emergence, the levels of use are highest during spring rainfall. This period is also the breeding season for most aquatic organisms.

EPA's risk assessment acknowledges a number of ways that atrazine may jeopardize endangered species (IRED at 66-67; Atrazine EFEC at 94-95). EPA's levels of concern for endangered terrestrial plants and vascular aquatic plants are exceeded (Atrazine EFEC at 94). Acute levels of concern for endangered species are exceeded for aquatic invertebrates, and chronic levels of concern are exceeded for fish and aquatic invertebrate reproduction (Atrazine EFEC at 95). Furthermore, EPA acknowledges that atrazine may indirectly affect endangered birds, mammals, and beneficial insects through loss of food sources and habitat disruption caused by atrazine's adverse chronic effects on terrestrial and aquatic plants (Atrazine EFEC at 94). Moreover, adverse effects of atrazine on aquatic vegetation may cause a loss of vegetative habitat that could affect populations of endangered aquatic invertebrates and endangered fish species (Atrazine EFEC at 95).

The U.S. Fish and Wildlife Service submitted extensive comments to EPA in response to the Atrazine EFEC, and FWS concluded that atrazine's release into the environment is

problematic (FWS Comments at 1). Chronic exposure may occur to a wide range of biota, because atrazine is persistent in aquatic environments and is transported via spray drift and runoff to surface water (FWS Comments at 2). FWS noted that EPA's risk assessment – which acknowledges significant ecological concerns – likely underestimates the "true potential for ecological impacts," in part because EPA did not consider sublethal effects of atrazine exposure, like the altered reproductive capacity of non-target organisms (FWS Comments at 2-3). FWS also disagreed with EPA's use of surrogate species for toxicity testing, pointing out that "standard test species" are not appropriate surrogates for listed species because "different species can have different life histories, biological requirements and sensitivities to pesticides . . . ." (FWS Comments at 3). FWS concluded that EPA's atrazine risk assessment process did not effectively address impacts to endangered species and did not appear to meet EPA's consultation requirement under the Endangered Species Act (FWS Comments at 7).

Section 7(a)(2) of the ESA requires that "each federal agency shall, in consultation with and with the assistance of the Secretary, insure that any action authorized, funded, or carried out by such agency (hereinafter in this section referred to as an 'agency action') is not likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of habitat of such species which is determined by the Secretary . . . to be critical." 16 U.S.C. §1536(a)(2). EPA has failed to consult with FWS and the National Marine Fisheries Service (NMFS), as required by Section 7(a)(2) of the ESA, 16 U.S.C. § 1536(a)(2), to ensure that its registration of the pesticide atrazine will not jeopardize the survival and recovery of endangered amphibians, reptiles, fish, birds, mammals, plants, aquatic invertebrates, and beneficial insects nationwide.

VIII. ATRAZINE HAS BEEN ASSOCIATED WITH AN INCREASED RISK OF CANCER IN SEVERAL STUDIES.

There is evidence from both epidemiology studies and laboratory studies suggesting that atrazine may be associated with an increased risk of cancer. Several laboratory studies have demonstrated that rats and mice exposed to atrazine had increased rates of uterine cancers, mammary tumors, and combined leukemia /lymphoma cancers[9] (note that these results are debated as to their significance to human risk). Several field studies of human exposure to triazine pesticides, including atrazine, find that exposure is associated with an increase in several cancer types: Hodgkins and Non-Hodgkins lymphoma,[10] colon cancer,[11] brain cancer,[12] testicular cancer,[13] and childhood cancers.[14] This is particularly disturbing given that childhood cancers (age 0-14 yrs) have risen 26% from 1975-1999.[15] NRDC insists that EPA provide a proper review of the available evidence suggesting an association between atrazine and cancer.

A. The St. Gabriel Study Sponsored by Syngenta Is Suggestive of a Cancer Link.

EPA concludes that an epidemiology study of workers at the Syngenta atrazine manufacturing plant (St. Gabriel study) was "insufficiently large and has limitations that

prevent ruling out atrazine as a potential contributor to the increase observed." (IRED at 49). In other words, despite Syngenta's efforts, the study fails to disprove the apparent link between atrazine exposure and increased cancer cases among workers. This is supported by further suggestive evidence, acknowledged by EPA in the IRED (at 49): "atrazine has also been tied to inflammation of the prostate in laboratory animals and changes in testosterone at high doses"; "other cancers besides prostate were found to have an elevated, though not statistically significant, increase in risk at the St. Gabriel plant"; "other studies have suggested an increased risk for ovarian, breast, and other cancers, including non-Hodgkin's lymphoma." NRDC agrees that the study is likely underpowered, but points out that insufficient statistical power predictably results in an underestimate of the magnitude of an association between an exposure and disease. In addition, the "healthy worker effect" predictably results in lower rates of chronic diseases such as cancer among active workers, making these results all the more unusual.

The St. Gabriel study was sent by the EPA to four reviewers, and, while one reviewer (Giovannucci) accepted the industry-authors suggestion that the excess in cancer was due to the company's PSA-screening initiative, the other three (Hayes, Morrison, Blair) were not so easily convinced. In fact, in contrast to Giovannucci, the other three epidemiologists all point out that no definite conclusions can be drawn, positive or negative, from such a weak study, and suggest improvements by which it might be more informative.[16]

1. Study summary.

The findings of the Syngenta/Novartis study of the atrazine manufacturing plant are presented in the Table below. All data is from the company study submitted to the EPA. Note that the company divided the cohort of workers into active and inactive employees, to designate whether they were currently employed by the plant, or former employees. The cohort was also divided into company and contract employees. Note that the excess in prostate cancers (11 v. 1.8) is in the active company employees, the same group that also received intensive PSA-screening. . Note also that the efforts to locate inactive employees and contract employees were exceptionally poor in this study. For example, the researchers made no efforts to locate inactive employees if they had moved out of Louisiana. This makes it quite possible, or even likely, that cases were missed in the inactive worker groups.

Observed/expected number of prostate cancers, by employee group, 1985-1999. Expected values are derived from comparison with the industrial corridor.[17]

	ACTIVE	*INACTIVE*	*TOTAL*
COMPANY	11/1.8	3/3.7	14/5.5
CONTRACT	1/1.1	2/3.0	3.0/4.1
TOTAL	12/2.9	5/5.6	17/9.5

2. Syngenta downplays atrazine's risks.

Although industry makes much of the fact that IARC has recently down-graded atrazine from group 2B (possible human carcinogen) to group 3 (unable to be classified), Dr. Morrison correctly points out the fact that this "hasn't been without controversy." Morrison refers to a published scientific article by NIEHS senior scientist James Huff, suggesting that atrazine is a victim of an increased reliance on industry data and increased industry representation on evaluation/advisory panels, resulting in a trend towards disregarding evidence of carcinogenesis.[18] Morrison challenges the industry assertion that there are no data to suggest carcinogenicity, stating, "to say that there is no prior biological or eidemiological evidence that atrazine is a human carcinogen is misleading. For an example of the non-existent epidemiological evidence, see [Schroeder et al, 1991]. Many other examples of positive epidemiological literature are cited by the review by the Natural Resources Defense Council." Morrison also points out that "[t]he [NRDC] review makes much of the finding of 11 cases, when 1.2 were expected, among company employees actively working at diagnosis. This is a *curious and suggestive finding, which isn't adequately dealt with in the paper by MacLennan et al.*" (emphasis added). And, although the industry provides very little exposure history of the cases, and none for the controls, they suggest that the lack of a clear dose-response should be interpreted as a lack of a causal association. Morrison disagrees, and asks, "[j]ust how much could you say about dose-response when you[r] study only has 11 cases?"

3. Tellingly, the authors of the Syngenta study have not attempted to provide quantitative estimates of the impact of PSA screening on prostate cancer incidence.

Dr. Hayes provides a suggestion for better quantifying the impact of PSA screening on prostate cancer incidence among this cohort, since the issue is germane to the interpretation of the data. He suggests that "further analysis of risk by calendar period, comparing PSA screening v. non-screening time-periods, could provide some insight into this important issue." Dr. Blair supports the need for this information by saying, "a few additional analyses of prostate cancer risk before and after initiation of screening would also provide direct information on the impact of the screening." NRDC suggests that it is both significant and curious that the manufacturer has made no attempt to quantify the impact of PSA screening on the cancer incidence, despite its confident assertions that PSA screening accounts for all the excess in prostate cancers.

4. Quantitative exposure assessment should be done for cases and controls.

Syngenta, after requests from NRDC and the EPA, provided some limited qualitative estimates of exposure for the prostate cancer cases. Dr. Aaron Blair states, "[t]o clearly understand the issue of prostate cancer and atrazine exposure in this cohort it is essential that a quantitative exposure assessment be added." Blair challenges the company to provide this information, saying, "[I]f it is possible to reconstruct possible atrazine exposure for cases, as was done for this report, it could be done for controls also."[19] Without proper case-control comparisons, Dr. Blair points out that the information about exposure among cases is not very informative. Morrison also raises concern about the

lack of this critical information, stating, "[t]he [NRDC] has correctly identified the lack of exposure histories of workers as both *significant and curious*." (emphasis added).

5. The industry-proposed nested case-control study is likely to be uninformative.

The reviewers expressed concern that the industry-proposed nested case-control study, would likely be uninformative due to the small number of cases, and without some design corrections. Dr. Blair states that "the small number of cases would be a severe limitation" to any case-control comparisons. Morrison states that "[t]he [industry] proposed nested case-control study lacks any discussion of the abysmal lack of power the study will realistically have. It would be a great study for the company to have conducted, given that it has little likelihood of observing a statistically significant effect because it will be underpowered." Hayes suggests that while "comparisons of exposure history of prostate cases and non-cases – coupled with individual data on PSA screening—could provide insight…" the Exponent proposal will be compromised from the small number of cases. Hayes suggests using the full cohort, or a random sample, to reconstruct risks.

6. The reviewers concluded that the study is underpowered and suffers methodological limitations, so that the contribution of atrazine to the observed excess cancers cannot be ruled out.

While the reviewers are clearly disappointed in the lack of effort to provide such important information as exposure histories for both cases and controls, they conclude that the study cannot rule out the possible association of atrazine with the observed excess in cancers. Morrison concludes, "while there was almost definitely some increased prostate cancer case finding because of the increased PSA screening, there was a suggestion that this might not be the entire explanation."[20] Hayes states "[w]hile PSA screening may account for much of the excess of prostate cancer in this Triazine manufacturing facility, it would be premature to reject a potential role of occupational exposure to triazines as a contributing factor to the observed excess of this disease."[21] NRDC concurs with the conclusions of the reviewers, that the study is underpowered and has some significant design problems. However, we do not think that these flaws are justification to completely ignore the results of this study. Instead, we believe the Agency must make every effort to work with Syngenta to update the new cancer cases through 2002, gather the additional exposure data on these workers, and to patch some of the other gaps in this study. In addition, EPA must consider this study in the context of all the evidence related to atrazine and cancer

NRDC again insists that the EPA must consider all the evidence, as required by the 2003 Draft Cancer Guidelines, in evaluating atrazine. While one or two weak studies may not be conclusive, the 2003 Guidelines dictate that a handful of weak epidemiology studies suggesting an association, coupled with evidence in animal studies, and with the evidence that there are at least two possible modes of action (LH disruption, aromatase activation), dictate that atrazine must be classified as a likely or suggested carcinogen.

B. Consistent with the 2003 Draft Cancer Guidelines, Atrazine Is a "Likely" or "Suggested" Human Carcinogen.

Atrazine has sufficient evidence of carcinogenicity in animal data, but insufficient evidence in humans, according to the International Agency for Research on Cancer (IARC).[22] A demonstrated mode of action is attenuation of leutenizing hormone (LH), which is hypothesized to explain the observed tumor response in rats, but is unlikely to induce tumor formation in humans. However, the recent decision by the EPA to classify it as "not likely" a human carcinogen is inconsistent with the 2003 Guidelines, and with the IARC criteria. The IARC states that the classification of "not a human carcinogen" requires a wealth of data, including multiple, mutually consistent, adequately powered studies covering the full range of human exposures that exclude with reasonable certainty bias, confounding, and chance to provide individual and pooled estimates of risk near unity with narrow confidence intervals.[23] Importantly, IARC cautions that latent periods substantially shorter than 30 years cannot provide evidence for lack of carcinogenicity (workers in the St. Gabriel study have a median of 18 years follow-up). *In no way should the absence of data be considered an absence of carcinogenicity.*

The 2003 Cancer Guidelines provide a framework for "judging whether available data support a mode of carcinogenic action hypothesized for an agent."[24] This framework incorporates the criteria for causality used in epidemiological studies, as stated by Bradford Hill (1965), with subsequent modifications. The author and those who use these criteria understand that each criterion support the determination of causality, and the more criteria that are satisfied, the stronger the evidence for causality. However, it is not necessary, and not likely, that all criteria are satisfied to demonstrate causality.[25] Further, the Guidelines remind the user that support for one mode of action does not limit the possibility of other modes of action. Rather, the Agency is obligated to consider the highly likely possibility of other modes of action that may be consistent with tumor formation in humans. For example, atrazine has been shown in animals and in human-derived cell cultures to stimulate aromatase activity, resulting in conversion of testosterone to estrogen. Might this mode of action cause or contribute to observed mammary tumors in male atrazine-exposed animals? The possibility, coupled with all existing experimental and epidemiological data,[26] would suggest that atrazine would more appropriately be classified as a "likely" or "suggested" human carcinogen, according to the 2003 Guidelines, and confirmed in conversations with EPA scientists W. Wood, W. Farland, and J. Cogliano.

IX. SUBSTANTIAL DATA DEMONSTRATE THAT ATRAZINE IS AN ENDOCRINE DISRUPTOR.

In establishing a tolerance for atrazine, EPA is expressly required to consider any effect "that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects." FFDCA §408(c)(2)(D)(viii), 21 U.S.C. §346(c)(2)(D)(viii). The evidence in laboratory animals of atrazine as an endocrine disruptor is particularly troublesome given that the highest tumor incidence among the U.S. population, regardless of race, is now prostate and breast cancers, both cancers of endocrine glands, and both showing

increasing incidence trends.[27] Dr. Hayes of the National Cancer Institute points out in his review for the EPA of the excess prostate cancers among workers in the atrazine manufacturing plant, that,

> [s]teroidal hormones are believed to play a role [in prostate cancer] because of their importance in prostate development, prostate cancer management, and their successful use in experimental disease induction. While testosterone and its metabolites are the prime suspects, inter-relationships in prostate carcinogenesis with estrogenic compounds may also be important. Atrazine and related compounds have profound estrogen disrupting capacity in amphibians at a very low dose [Hayes et al, 2002][28]

Atrazine disrupts sexual development in experimental animals. When nursing rats were treated with atrazine the male offspring developed prostate gland inflammation[29] (note, this study was done by EPA staff scientists). It is not known if prostatitis will proceed to prostate cancer. Treatment of rats with atrazine from weaning until puberty resulted in delayed sexual maturity[30] (note, this study was done by EPA staff scientists). Atrazine reduced the ability of active testosterone to bind to its receptor in the prostate gland, thus reducing its effectiveness.[31] Atrazine reduced the ability of testosterone to convert to its active form in rat prostate gland.[32] Atrazine has been shown to be toxic to sperm, and reduced sperm motility in exposed rats.[33]

Atrazine acts in amphibians to disrupt reproductive organ development. The following summary of supporting data is excerpted from unpublished notes compiled by Dr. Tyrone Hayes, Berkeley Univ, CA. Following exposure to 21 ppb (μg/L) for only 48 hours, atrazine-exposed *Xenopus laevis* (frog) males suffered from testicular resorption that resulted in gonadal dysgenesis (small underdeveloped testis with decreased germ cell numbers).[34] Effects were quite significant and included a 57% reduction in testicular volume, a 70% reduction in primary spermatogonial cell nests (which represent the germ cells for the life of the organism), a 74% reduction in the nurse cells (which represent the pool of sperm-nourishing cells for the organism's life), testicular resorption in 70% of the exposed males, and failure of full development in 10% of the exposed males. Atrazine induced feminization of male gonads in *X. laevis*; hermaphroditism and gonadal dysgenesis occurred in 16-20% of the exposed frogs (32-40% of the males).[35] In similar studies in wild *Rana pipiens* (frogs), testicular oocytes were observed at 0.1 and 25 μg/L atrazine at all sites where water-concentrations of atrazine was measured in excess of 0.1 μg/L.[36] [37] The observed gonadal abnormalities associated with atrazine exposure in amphibians are of great concern: 32-40% of the males in *X. laevis,* up to 29% of the male *Rana pipiens* in the laboratory and up to 92% of the males in some wild populations. Further, Syngenta-funded researchers James Carr and others treated *X. laevis* larvae throughout development.[38] "Carr *et al*. (2003) report a concentration-dependent relationship between atrazine and total incidence of gonadal abnormalities males."[39] Another recent study funded by Syngenta found hermaphroditic *Bufo marinus* (cane toads) in sugarcane fields treated with atrazine, but no hermaphroditism at reference sites free of atrazine.[40] In fact, males in contaminated areas had female-typical skin coloration, had measurable vitellogenin in the plasma and some had eggs.[41] It was

reported that this work "lends credence to University of Berkeley endocrinologist Tyrone Hayes' hypothesis that atrazine is affecting sexual development of amphibians," and Syngenta-funded researcher Tim Gross was cited "adding that the findings are consistent with the previous work of both Hayes and Texas Tech experimental toxicologist James Carr, 'Carr finds an effect at atrazine concentrations that are similar to what we see in the field and to what we think the toads are exposed.'"[42]

Thus, there is compelling evidence for endocrine effects from multiple, mutually-consistent studies in multiple species, with sufficient statistical power. There is compounding and compelling evidence for multiple mechanisms of action of atrazine and all are consistent with the observed effects of atrazine on reproductive development and function in mammals and amphibians. Many agencies have identified atrazine as an endocrine disruptor, including the United Kingdom's Environmental Agency, the European Union, the Oslo and Paris Commission Convention for the Protection of the Marine Environment of the North-East Atlantic, and the State of Illinois. These findings, along with the evidence noted above, compel a finding of unreasonable adverse effects on the environment under FIFRA, and cancellation of atrazine.

Under FFDCA §408, moreover, EPA cannot determine a "safe" level of atrazine at which there is a "reasonable certainty of no harm" to infants, children, and vulnerable populations from the endocrine disrupting effects of atrazine, and therefore the agency simply cannot leave in effect any tolerances for atrazine under FFDCA §408. If there is a threshold for atrazine's endocrine effects, EPA has not found it, and therefore EPA can allow no greater than a 1 in 1 million risk of any endocrine disrupting effect to exposed individuals under the FFDCA. If EPA had found a threshold for atrazine's endocrine effects, the agency would have to scientifically explain and justify that threshold determination, and apply that in determining whether any tolerance could legally issue, using appropriate safety factors (including the statutory tenfold safety factor to protect infants and children).

X. CONCLUSION.

EPA's Atrazine IRED is significantly flawed. The IRED both understates legitimate risks from atrazine exposure (such as the endocrine effects) and ignores the risks that it does acknowledge (such as the ecological harm and jeopardy to endangered species). In light of the above comments, EPA cannot reregister atrazine without violating the Agency's obligation under FIFRA to prevent unreasonable adverse effects on human health and the environment. FIFRA §§ 3(c)(5) & 4(g)(2).

EPA and NRDC resolved litigation in *NRDC v. Whitman*, No. C-99-3701 WHA (N.D. Cal.), through a consent decree. Pursuant to the amended consent decree between EPA and NRDC in that case, affirmed by court order on January 24, 2003, EPA must sign a revised Atrazine IRED by October 31, 2003. The consent decree also obligates EPA to submit a paper to the FIFRA Scientific Advisory Panel (SAP) for review and comment concerning (1) the significance of amphibian risk data; (2) whether there is a need for additional data to characterize more fully atrazine's potential risks to amphibians; and (3)

other scientific issues concerning atrazine, including "the significance of data bearing on the association between atrazine exposure and the incidence of prostate or other cancer in humans." EPA must develop this paper and submit it to the SAP for review and comment by July 31, 2003 – three months before the October 31 revised IRED deadline. NRDC fully expects that EPA will do so, and we will treat any failure to do so as a breach of the consent decree in contempt of court.

Please feel free to contact us at (202) 289-6868 should you have any questions about these comments. Thank you for the opportunity to comment, and thank you in advance for your consideration.

Respectfully submitted,

Jennifer Sass, Ph.D. Senior Scientist	Aaron Colangelo Staff Attorney	Erik D. Olson Senior Attorney	Gina Solomon, M.D. Senior Scientist

[1] Atrazine: Response to Public Comments on the EPA's April 16, 2002 Revised Human Health Risk Assessment and Associated Documents for the Reregistration Eligibility Decision (RED). PC Code: 080803. DP Barcode: 284707. January 31, 2003

[2] NRDC comments to EPA on the revised human health assessment for atrazine. July, 2002. Docket # OPP-34237C

[3] Katten, A. California Rural Legal Assistance Foundation. Presentation. A view from the field: Use and limitations of incident data. Worker Risk Seminar, October, 2002.

Fenske, R. Univ Washington. Towards more accurate assessments of occupational pesticide exposure. Worker Risk Seminar, October, 2002.

[4] California Environmental Protection Agency, Department of Pesticide Regulation. Compliance Assessment Report (Pesticide Handler and Field Worker Safety Survey, June 1997--March 2001). http://www.cdpr.ca.gov/docs/enfcmpli/cmpasses.pdf

[5] Blondell, J.EPA. Presentation. Use of incident data in exposure evaluation. Worker Risk Seminar, October, 2002.

Calvert, GM. NIOSH-CDC. Presentation. An overview of SENSOR-pesticides tracking acute occupational pesticide-related illness in the US. Worker Risk Seminar, October, 2002.

[6] Reregistration Eligibility Science Chapter for Atrazine, Environmental Fate and Effects Chapter, p. 1 (Jan. 26, 2001).

[7] Kettle WD, deNoyelles F Jr, Heacock BD, Kadoum AM. Diet and reproductive success of bluegill recovered from experimental ponds treated with atrazine. Bull Environ Contam Toxicol 1987 Jan;38(1):47-52. MRID

[8] Kettle et al, ibid.

[9] Pinter A, Torok G, Borzsonyi M, et al. Long-term carcinogenicity bioassay of the herbicide atrazine in F344 rats. *Neoplasma*. 1990;37(5):533-44.

Stevens JT, Breckenridge CB, Wetzel L. A risk characterization for atrazine: oncogenicity profile. *J Toxicol Environ Health A*. 1999;56(2):69-109.

Donna A, Betta PG, Robutti F, Bellingeri D. Carcinogenicity testing of atrazine: preliminary report on a 13-month study on male Swiss albino mice treated by intraperitoneal administration. *G Ital Med Lav*. 1986;8(3-4):119-21.

[10] Hoar SK, Blair A, Holmes FF, et al. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. *Jama*. 1986;256(9):1141-7.

Zahm SH, Weisenburger DD, Saal RC, Vaught JB, Babbitt PA, Blair A. The role of agricultural pesticide use in the development of non- Hodgkin's lymphoma in women. *Arch Environ Health*. 1993;48(5):353-8.

Schroeder JC, Olshan AF, Baric R, et al. Agricultural risk factors for t(14;18) subtypes of non-Hodgkin's lymphoma. *Epidemiology*. 2001;12(6):701-9.

[11] Hoar SK, Blair A, Holmes FF, Boysen C, Robel RJ. Herbicides and colon cancer. *Lancet*. 1985;1(8440):1277-8.

[12] Mills PK. Correlation analysis of pesticide use data and cancer incidence rates in California counties. *Arch Environ Health*. 1998;53(6):410-3.

[13] Mills PK. Correlation analysis of pesticide use data and cancer incidence rates in California counties. *Arch Environ Health*. 1998;53(6):410-3.

[14] Daniels JL, Olshan AF, Savitz DA. Pesticides and childhood cancers. *Environ Health Perspect*. 1997;105(10):1068-77.

[15] SEER Cancer Statistics Review 1973-1999. National Cancer Institute. Section XXVII, Childhood cancer by site, incidence, survival, and mortality.

[16] Blondell, J. EPA. Review of additional data on potential atrazine exposure and review comments submitted by Syngenta and NRDC on atrazine cancer epidemiology study: "Follow-up study of cancer incidence among workers in triazine-related operations at the Novartis St. Gabriel plant" by Elizabeth Delzell et al. DP Barcode D287278, MRID#455184-01. January 15, 2003

[17] Delzell E, Sathiakumar N, MacLennan P, Grizzle W, Cheng H. 2001. A follow-up study of cancer incidence among workers in triazine-related operations at the Novartis St. Gabriel plant. Syngenta Number 2207-01. Data taken from Tables 17, 18.

[18] Huff J. IARC monographs, industry influence, and upgrading, downgrading, and under-grading chemicals: a personal point of view. International Agency for Research on Cancer. *Int J Occup Environ Health*. 2002;8(3):249-70

[19] op cit. Blondell, 2003. p. 27

[20] op cit. Blondell, 2003. p. 17

[21] op cit. Blondell, 2003. p. 23

[22] IARC. Atrazine. *International Agency for Research on Cancer Monogr Eval Carcinog Risks Hum*. Vol 73, 1999.

[23] Melnick RL, Kamel F, Huff J. 2003. Declaring chemicals "not carcinogenic to humans" requires validation, not speculation. Environ Health Perspect, 111 (4); A204

[24] Draft Cancer guidelines. 2003. p. 2-31. Section 2.5.3

[25] Draft Cancer guidelines. 2003. p. 2-31, lines 30-32

[26] Hoar SK, Blair A, Holmes FF, Boysen CD, Robel RJ, Hoover R, et al. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. Jama 1986;256(9):1141-7.

Zahm SH, Weisenburger DD, Saal RC, Vaught JB, Babbitt PA, Blair A. The role of agricultural pesticide use in the development of non- Hodgkin's lymphoma in women. Arch Environ Health 1993;48(5):353-8.

Schroeder JC, Olshan AF, Baric R, Dent GA, Weinberg CR, Yount B, et al. Agricultural risk factors for t(14;18) subtypes of non-Hodgkin's lymphoma. Epidemiology 2001;12(6):701-9.

Hoar SK, Blair A, Holmes FF, Boysen C, Robel RJ. Herbicides and colon cancer. Lancet 1985;1(8440):1277-8

Mills PK. Correlation analysis of pesticide use data and cancer incidence rates in California counties. Arch Environ Health 1998;53(6):410-3.

MacLennan PA, Delzell E, Sathiakumar N, Myers SL, Cheng H, Grizzle W, Chen VW, Wu XC. Cancer incidence among triazine herbicide manufacturing workers. J Occup Environ Med. 2002 Nov;44(11):1048-58.

Mills PK. Correlation analysis of pesticide use data and cancer incidence rates in California counties. Arch Environ Health 1998;53(6):410-3.

Daniels JL, Olshan AF, Savitz DA. Pesticides and childhood cancers. Environ Health Perspect 1997;105(10):1068-77.

Pinter A, Torok G, Borzsonyi M, Surjan A, Csik M, Kelecsenyi Z, et al. Long-term carcinogenicity bioassay of the herbicide atrazine in F344 rats. Neoplasma 1990;37(5):533-44.

Stevens JT, Breckenridge CB, Wetzel L. A risk characterization for atrazine: oncogenicity profile. J Toxicol Environ Health A 1999;56(2):69-109.

Donna A, Betta PG, Robutti F, Bellingeri D. Carcinogenicity testing of atrazine: preliminary report on a 13-month study on male Swiss albino mice treated by intraperitoneal administration. G Ital Med Lav 1986;8(3-4):119-21.

Hayes T, Haston K, Tsui M, Hoang A, Haeffele C, Vonk A. Herbicides: Feminization of male frogs in the wild. Nature 2002;419(6910):895-6.

Hayes TB, Collins A, Lee M, Mendoza M, Noriega N, Stuart AA, et al. Hermaphroditic, demasculinized frogs after exposure to the herbicide atrazine at low ecologically relevant doses. Proc Natl Acad Sci U S A 2002;99(8):5476-80.

Stoker TE, Robinette CL, Cooper RL. Maternal exposure to atrazine during lactation suppresses suckling-induced prolactin release and results in prostatitis in the adult offspring. Toxicol Sci 1999;52(1):68-79.

Stoker TE, Laws SC, Guidici DL, Cooper RL. The effect of atrazine on puberty in male wistar rats: an evaluation in the protocol for the assessment of pubertal development and thyroid function. Toxicol Sci 2000;58(1):50-9.

Laws SC, Ferrell JM, Stoker TE, Schmid J, Cooper RL. The effects of atrazine on female wistar rats: an evaluation of the protocol for assessing pubertal development and thyroid function. Toxicol Sci 2000;58(2):366-76.

Danzo BJ. Environmental xenobiotics may disrupt normal endocrine function by interfering with the binding

of physiological ligands to steroid receptors and binding proteins. Environ Health Perspect 1997;105(3):294-301.

Friedmann, AS. Atrazine inhibition of testosterone production in rat males following peripubertal exposure. Reprod Toxicol. 2002 May-Jun;16(3):275-9.

Kniewald J, Jakominic M, Tomljenovic A, Simic B, Romac P, Vranesic D, et al. Disorders of male rat reproductive tract under the influence of atrazine. J Appl Toxicol 2000;20(1):61-8

[27] United States Cancer Statistics. 1999 report. National Cancer Institute and the Center for Disease Control and Prevention.

[28] Op cit. Blondell, 2003. p. 23

[29] Stoker TE, Robinette CL, Cooper RL. Maternal exposure to atrazine during lactation suppresses suckling-induced prolactin release and results in prostatitis in the adult offspring. *Toxicol Sci*. 1999;52(1):68-79.

[30] Stoker TE, Laws SC, Guidici DL, Cooper RL. The effect of atrazine on puberty in male wistar rats: an evaluation in the protocol for the assessment of pubertal development and thyroid function. *Toxicol Sci*. 2000;58(1):50-9.

Laws SC, Ferrell JM, Stoker TE, Schmid J, Cooper RL. The effects of atrazine on female wistar rats: an evaluation of the protocol for assessing pubertal development and thyroid function. *Toxicol Sci*. 2000;58(2):366-76.

[31] Danzo BJ. Environmental xenobiotics may disrupt normal endocrine function by interfering with the binding of physiological ligands to steroid receptors and binding proteins. *Environ Health Perspect*. 1997;105(3):294-301.

[32] Kniewald J, Osredecki V, Gojmerac T, Zechner V, Kniewald Z. Effect of s-triazine compounds on testosterone metabolism in the rat prostate. *J Appl Toxicol*. 1995;15(3):215-8.

[33] Kniewald J, Jakominic M, Tomljenovic A, et al. Disorders of male rat reproductive tract under the influence of atrazine. *J Appl Toxicol*. 2000;20(1):61-8

[34] Tavera-Mendoza L, Ruby S, Brousseau P, Fournier M, Cyr D, Marcogliese D. Response of the amphibian tadpole (Xenopus laevis) to atrazine during sexual differentiation of the testis. *Environ Toxicol Chem*. 2002;21(3):527-31.

[35] Hayes TB, Collins A, Lee M, Mendoza M, Noriega N, Stuart AA, Vonk A. Hermaphroditic, demasculinized frogs after exposure to the herbicide atrazine at low ecologically relevant doses. Proc. Natl. Acad. Sci. USA 99, 5476-5480 (2002).

[36] Hayes TB, Haston K, Tsui M, Hoang A, Haeffele C, Vonk A. Feminization of male frogs in the wild. Nature 419: 895-896 (2002)

[37] Hayes TB, Haston K, Tsui M, Hoang A, Haeffele C, Vonk A. Atrazine-induced hermaphroditism at 0.1 ppb in American leopard frogs (*Rana* pipiens): Laboratory and field evidence. Environ. Health Perspect. *In press.* (2002).

[38] Carr JA, Gentles A, Smith EE, Goleman WL, Urquidi LJ, Thuett K, Kendall RJ, Giesy JP, Gross, TS, Solomon, KR, Van Der Kraak, G. Response of larval *Xenopus laevis* to atrazine: Assessment of growth, metamorphosis, and gonadal and laryngeal morphology. *Environ Toxicol Chem.* 22: 396-405 (2003).

[39] Carr JA, Solomon KR. Is atrazine causing frog deformities at very low doses? Setac Globe. 4: 30-32. (2003).

[40] Mckoy KA, Sepulveda MS, Gross TS. Atrazine exposure and reproductive system abnormalities in field collected *Bufo marinus*. Abstract, 23rd Annual Meeting in North America, Soc. Environ. Toxicol. Chem., Salt Lake City, UT (2002).

[41] Mckoy KA, Sepulveda MS, Gross TS. Atrazine exposure and reproductive system abnormalities in field collected *Bufo marinus*. Abstract, 23rd Annual Meeting in North America, Soc. Environ. Toxicol. Chem., Salt Lake City, UT (2002).

[42] Renner R. More evidence that herbicides feminize amphibians. Environ. Science Tech. 46A (2002)