ATTACHMENT B

NRDC, *Atrazine Detailed Evaluation Letter*
(June 3, 2002)

NRDC
THE EARTH'S BEST DEFENSE

NATURAL RESOURCES DEFENSE COUNCIL

June 3, 2002

Mr. Stephen L. Johnson
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Office of Prevention, Pesticides, and Toxic Substances
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Public Information and Records Integrity Branch
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Environmental Protection Agency,
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Washington, DC 20460
Attn: Docket # OPP-34237C

Dear Mr. Johnson:

Enclosed please find the Natural Resources Defense Council's detailed evaluation of a number of critical scientific, policy, and legal issues central to EPA's upcoming assessment of atrazine's eligibility for reregistration under the Federal Insecticide, Fungicide and Rodenticide Act and the Agency's reassessment of applicable food tolerances under the Federal Food, Drug and Cosmetic Act.

This notice demonstrates clearly that atrazine should be taken off the market. New scientific evidence shows that workers in an atrazine manufacturing plant developed prostate cancer at high rates, and laboratory experiments show that atrazine-exposed frogs develop severe sexual deformities at levels 30 times lower than EPA's drinking water standard. In short, the chemical is more dangerous than previously believed. Also, EPA's risk assessment depends in part on an unlawful and unethical experiment in which human volunteers were intentionally exposed to atrazine, and EPA's stated policy is to reject such studies.

Considering the new science, existing studies linking atrazine to breast, blood, and other cancers, and the fact that atrazine appears commonly in drinking water, frequently in violation of applicable standards, NRDC calls on EPA to join several European nations and ban atrazine.

Sincerely,

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ATRAZINE: AN UNACCEPTABLE RISK TO AMERICA'S CHILDREN & ENVIRONMENT

AGGREGATE EXPOSURE TO ATRAZINE RESIDUES IS NOT SAFE FOR CHILDREN AND PREGNANT WOMEN AND ALSO POSES AN UNREASONABLE RISK TO HUMAN HEALTH AND THE ENVIRONMENT. MOREOVER, ALTHOUGH NO EPA FINDING WITH RESPECT TO ATRAZINE'S BENEFITS IS REQUIRED, SAFER ALTERNATIVES ARE AVAILABLE

SIGNIFICANT NEW DEVELOPMENTS NECESSITATE CHANGES TO THE HUMAN HEALTH AND ENVIRONMENTAL RISK ASSESSMENTS FOR ATRAZINE

The Natural Resources Defense Council (NRDC) has repeatedly voiced serious concerns about the health and environmental effects of the pesticide atrazine. In this notice, we hereby urge EPA to consider not only the enormous accumulation of past evidence of the health and environmental threats posed by atrazine, but also to revise its assessment of these threats in light of significant new data. Together, these data present compelling evidence that EPA has a scientific and legal duty to remove atrazine from the market.

Thousands of our members live in areas where the environment and water are contaminated with this hazardous chemical. Atrazine is the most widely used herbicide in the United States, with over 60 million pounds applied annually. Drinking water in many areas throughout the U.S. is polluted with this chemical. In particular, surface water sampling in agricultural areas commonly detects exceedances of the applicable Safe Drinking Water Act maximum contaminant level (MCL) of 3 parts per billion (ppb);

indeed, according to data from atrazine's primary registrant, Syngenta, over one million Americans have, in recent years, consumed tap water that exceeded EPA's MCL.[1] Atrazine has even been reported in rainfall at levels well in excess of 3 ppb.[2] In addition, short-term peaks in atrazine concentrations are far higher than the drinking water benchmark during the spring and early summer.[3] Even without the new scientific data discussed in this notice, the violations of the atrazine drinking water standard are extremely worrisome, and alone constitute grounds for revocation of atrazine's tolerances because the aggregate exposure to atrazine cannot be found to be "safe" under applicable law.[4]

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[1] Data provided by atrazine's manufacturer to the EPA atrazine reregistration docket reveals that 1,107,141 people received water from a drinking water system that had at least one annual violation of the MCL in the years 1993-1998. *See* U.S. EPA, Drinking Water Exposure Assessment For Atrazine And Various Chloro-Triazine And Hydroxy-Triazine Degradates, Sub-Appendix A-2 (Jan. 23, 2001), available online at http://www.epa.gov/pesticides/reregistration/atrazine/drinkingwater_a2.pdf (visited May 9, 2002); *see also* U.S. Geological Survey, Pesticides in Surface and Ground Water of the United States: Summary of Results of the National Water Quality Assessment Program, Table 1 (July 22, 1998) (finding atrazine in 78.66 percent of samples taken), available online at http://ca.water.usgs.gov/pnsp/allsum/#t1 (visited May 16, 2002); 59 Fed. Reg. 60,412, 60,425 (Nov. 23, 1994) ("The available data suggest that a number of surface source drinking water supply systems within the corn belt will have annual average atrazine concentrations exceeding the atrazine MCL"); Environmental Working Group & Physicians for Social Responsibility, *Tap Water Blues*, at 116-17 & fig. 14 (1994) (in Illinois, 9 water systems exceeded 3 ppb annually and 10 percent of all samples taken exceeded 3 ppb); *id.* at 133 (in Indiana, 25 percent of samples taken exceeded 3 ppb); *id.* at 156 & fig. 29 (in Iowa, 2 water systems exceeded 3 ppb annually); *id.* at 169, 171, & fig. 34 (in Kansas, 11 percent of samples taken exceeded 3 ppb and 1 water system exceeded 3 ppb annually).

[2] *See, e.g.*, U.S. Geological Survey, "Herbicides in Rainfall Across the Midwestern and Northeastern United States, 1990-91," available online at http://ks.water.usgs.gov/Kansas/pubs/fact-sheets/fs.181-97.html#HDR1 (visited April 11, 2002).

[3] *See* U.S. Geological Survey, "Herbicides in streams and major rivers were highest in the most intensively farmed agricultural regions," available online at http://water.usgs.gov/pubs/circ/circ1225/html/intensively.html (visited April 10, 2002); *see also Tap Water Blues, supra* note 1 at 169, table 56 (high monitored concentration of 105 ppb).

[4] Although this is a notice primarily focused on important new scientific information, NRDC notes that regular violations of the MCL render atrazine legally ineligible for reregistration under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and prohibit EPA from issuing a tolerance for atrazine residues on food under the Federal Food, Drug and Cosmetic Act (FFDCA). Under the FFDCA, EPA may only issue a tolerance – a legally-permissible level of residue in food – if it is "safe," and a tolerance is only "safe" if "there is a reasonable certainty that no harm will result from *aggregate exposure* to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." 21 U.S.C. § 346a(b)(2)(ii) (emphasis added). Thus, EPA must find that total

Millions of people, as well as animals (including endangered amphibians), are currently exposed to this pesticide due to direct use, drift, and water contamination. Bottle-fed infants whose formula is reconstituted using tap water are among those exposed.[5] These infants, along with pregnant women, are exposed to "pulses" of particularly high levels of atrazine in the late spring when runoff into surface water contaminates many drinking water supplies. For a developmental toxicant and endocrine disruptor such as atrazine, short-term exposures to high levels are a significant concern, because irreversible effects can occur after relatively brief exposures during vulnerable developmental periods.

Recent scientific data add to existing information showing serious health and environmental risks from this chemical. Prior research demonstrates that atrazine causes cancer of the mammary glands in at least one strain of rat. The chemical interferes with

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exposure to atrazine from all sources, including drinking water, is "safe," or it must revoke all of atrazine's tolerances. FIFRA specifies that pesticides may not be reregistered if the risk from dietary exposures to the pesticide residue is unsafe under the FFDCA. *See* 7 U.S.C. § 136a-1(g)(E) (requiring EPA to examine the risk from dietary exposures in reregistration process); *id.*§§ 136a-1(a)(2) & 136a(c)(5) (allowing reregistration only if pesticide, "will not generally cause unreasonable adverse effects on the environment"); *id.* §136(bb) (defining "unreasonable adverse effects on the environment" to include "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard in" the FFDCA). Because reregistration and tolerance approval is appropriate only if exposures to pesticide residues are "safe," and because drinking water in excess of the MCL is by definition not safe, *see* 42 U.S.C. § 300g-1(b)(4)(B) (defining MCL to be the level "as close to the maximum contaminant level goal [(MCLG)] as is feasible"); *id.* § 300g-1 (b)(4)(A) (defining MCLG to be "the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety"), EPA must revoke all tolerances for atrazine and may not reregister atrazine or approve any new tolerance for atrazine.

[5] *See* Environmental Working Group, "Tough to Swallow: How Pesticide Companies Profit from Poisoning America's Tap Water," (1997), available online at http://www.ewg.org/reports/toughtoswallow/dw.pdf (visited May 30, 2002). For further detail about herbicides in drinking water, see Environmental Working Group, Natural Resources Defense Council & Environmental Information Center, "Just Add Water," (1996) available online at http://www.ewg.org/reports/JustAddWater/JustAdd.html (visited May 30, 2002); Environmental Working Group, "Weed Killers by the Glass," (1995), available online at http://www.ewg.org/reports/Weed_Killer/Weed_Home.html (visited May 30, 2002); Environmental Working Group, "Setting the Record Straight," (1995), available online at http://www.ewg.org/reports/setting_straight/setting_intro.html (visited May 30, 2002).

numerous hormones and has adverse effects on reproduction and development. In particular, atrazine causes prostate inflammation, delayed puberty, altered lactation, disrupted estrous cycling, and decreased sperm production in rodent studies. More recent data show that atrazine-contaminated water can prevent normal reproductive organ development in frogs, even at extremely low doses. Further, an epidemiological study generated by the manufacturer shows an alarmingly high rate of prostate cancer in atrazine-exposed workers.

In addition to new empirical data, EPA's prior risk assessment of atrazine needs to be corrected to account for the Agency's policy decision not to consider data from tests in which human subjects are intentionally dosed with pesticides, and its recent statement affirming this position while the National Academy of Sciences considers the moral and ethical implications of conducting such tests. Because a scientifically invalid and morally and legally unacceptable experiment on humans provides the basis for EPA's underestimation of the amount of atrazine that penetrates the skin when a person is exposed to the chemical, the human health assessment understates the risk of atrazine poisoning.

This notice is based on the entire toxicologic record amassed to date at EPA on atrazine. However, the important new studies discussed below and EPA's policy not to accept human testing makes the Agency's prior health assessment of atrazine inadequate. The compound is more hazardous than previously believed, and these new facts indicate the need for immediate action to revoke all tolerances for atrazine and to cancel it.

Brief Summary of Atrazine's Health Effects

EPA has concluded that atrazine has low acute toxicity. The main concerns about atrazine include cancer and endocrine disruption. Atrazine repeatedly has been shown to cause cancers of the mammary glands (breast) in rats.[6] In humans, several studies have indicated possible links between cancers of the breast, ovaries, and prostate, and history of exposure to atrazine.[7] There is also a possible link between atrazine and Non-Hodgkin's lymphoma.[8]

Atrazine does not seem to bind directly to hormone receptors. Instead, this chemical acts indirectly, in various ways, on sex hormones. Atrazine seems to block release of a "master hormone" (gonadotropin releasing hormone) from the "master gland," the hypothalamus.[9] This blockage results in suppression of hormone release from the pituitary gland and a cascade of hormonal effects on the ovaries and other glands. Atrazine also speeds-up the conversion of androgens to estrogens, a process that can lead to elevated estrogen levels and may predispose people to breast cancer.[10] Finally, atrazine may alter the metabolism of estrogen, and create higher levels of a harmful estrogen

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[6] Stevens JT, Breckenridge CB, Wetzell LT, Gillis JH, Luempert LG, Eldridge JC. Hypothesis for mammary tumorigenisis in Sprague-Dawley rats exposed to certain triazine herbicides. J of Toxicol and Environ Health 43:139-53, 1994; Donna A, Crosignani P, Robutti F, Betta PG, Bocca R, Mariani N, Ferrario F, Fissi R, Berrino F. Triazine herbicides and ovarian epithelial neoplasms. *Scand J Work Environ Health* 1989;15:47-53.

[7] *See, e.g.*, Kettles MK, Browning SR, Prince TS, Horstman SW, Triazine herbicide exposure and breast cancer incidence: an ecologic study of Kentucky counties, 105 Environmental Health Perspectives 1222-7 (1997).

[8] Cantor KP, Blair A, Everett G, Gibson R, Burmeister LF, Brown LM, Schuman L, Dick FR, Pesticides and other agricultural risk factors for non-Hodgkin's lymphoma among men in Iowa and Minnesota, 52 Cancer Research 2447-55 (1992).

[9] Cooper RL, Goldman JM, Stoker TE., Neuroendocrine and reproductive effects of contemporary-use pesticides, 15 Toxicol Indust Health 26-36 (1999).

[10] Sanderson JT, Seinen W, Giesy JP, van den Berg, 2-Chloro-s-triazine herbicides induce aromatase (Cyp19) activity in H295R human adrenocortical carcinoma cells: a novel mechanism for estrogenicity?, 54 Toxicol. Sciences 121-127 (2000).

metabolite (16-alpha-hydroxyestrone).[11] All of these hormonal actions may contribute to cancers of hormonally-responsive tissues, and to developmental abnormalities.

Endocrine Disrupting Effects in Amphibians at Low Doses

Research recently published in the prestigious *Proceedings of the National Academy of Sciences* by Dr. Tyrone Hayes and colleagues at the University of California, Berkeley, has revealed serious reproductive effects of atrazine in male frogs.[12] These effects occur at very low doses, at or below levels commonly found in the environment. In addition, the harms Dr. Hayes observed appear to occur through a mode of action that EPA has not previously considered in its draft risk assessment. Males with such sexual abnormalities are unlikely to be able to reproduce efficiently, if at all. This new research and its potential implications for human health is sufficient to warrant reducing or discontinuing atrazine use.

Frogs exposed in the laboratory to water contaminated with atrazine at levels as low as 0.1 part-per-billion (ppb), a full 30 times lower than the current allowable drinking water standard, experienced abnormal sexual maturation. In Dr. Hayes's experiments, 16 to 20 percent of the individual animals developed multiple gonads or had both testes and ovaries, at exposure levels of 0.1 ppb.[13] Similarly, when exposed to 1 ppb atrazine, male

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[11] Bradlow HL, Davis DL, Lin G, Tiwari R, Effects of pesticides on the ratio of 16 alpha/2-hydroxyestrone: a biologic marker of breast cancer risk, 103 Environ. Health Perspect. 147-50 (1995).
[12] 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, 99 PNAS 5,476 (April 16, 2002).
[13] *Id.* at 5,477.

frogs had abnormally small laryngeal muscles,[14] which would likely hinder their ability to produce effective mating calls.

As discussed above, atrazine routinely pollutes lakes, rivers, and streams, and drinking water at levels far greater than those tested in Dr. Hayes's laboratory. Because doses of atrazine one-thirtieth of the legal drinking water level disrupted gonadal development in one out of every six frogs tested, Dr. Hayes's research has frightening implications for people drinking this water, especially pre-pubescent children,. Alteration in sexual development in frogs suggests that atrazine could cause hormonal disruption in humans.

Field studies confirm that atrazine's effects are not confined to laboratory experiments. Following his lab work, Dr. Hayes studied wild frogs living in agricultural areas where atrazine is applied and found comparable gonadal abnormalities. The U.C. Berkeley researchers collected frogs from water bodies in the Midwest and tested the water for pesticide residues. The findings in these amphibians were similar to the findings in the laboratory, with reproductive abnormalities appearing in wild frogs.[15]

The frog studies are shocking in two respects. First, as discussed above, they reveal serious effects at environmentally relevant – indeed, routine – conditions. Second, the findings indicate that atrazine acts in the body in a way that EPA has to date ignored. Dr. Hayes's results are most consistent with a mode of action other than the one previously proposed by EPA. In earlier risk assessments for atrazine, EPA cited mode of action evidence indicating that atrazine causes hypothalamic disruption of gonadotropin

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[14] *Id.*

releasing hormone (GnRH), resulting in critical reductions in pituitary luteinizing hormone (LH) and resultant failure of ovulation in females. This mode of action fails to account for the effects seen at low doses in frogs. If the hypothalamus were affected (as EPA suggests), then the thyroid gland would also be affected, since its activity is regulated by the hypothalamus. However, in Dr. Hayes's work, there is no disruption of thyroid-dependent effects, such as growth and metamorphosis.

The results of the frog studies suggest that atrazine causes harm via an additional mechanism beyond what EPA supposes. Dr. Hayes proposes that atrazine stimulates aromatase activity in male frogs' testes – the active aromatase acts to convert testosterone to estrogen, thus resulting in a reduction in testosterone, and feminization of the gonads.[16] In addition, Dr. Hayes's observations of male frogs' laryngeal muscles is consistent with this hypothesized mechanism; this muscle, which was abnormally small in exposed frogs, is testosterone-dependent for its growth. Finally, Dr. Hayes's suggested mechanism of action is supported by other research demonstrating that atrazine induces aromatase activity in animals and in human cell lines.[17]

Because humans also have the aromatase enzyme, increased aromatase production in humans could have similar results to those seen in the frogs; lower levels of male androgens and higher levels of estrogens in both sexes. These hormonal alterations could

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[15] Press Release, "Popular Weed Killer Demasculinizes Frogs, Disrupts Their Sexual Development, UC Berkeley Study Shows" (April 15, 2002).
[16] Hayes et. al, *supra* note 12, at 5,478.
[17] Sanderson JT, Letcher RJ, Heneweer M, Giesy JP, van den Berg M. Effects of chloro-s-triazine herbicides and metabolites on aromatase activity in various human cell lines and on vitellogenin production in male carp hepatocytes, 109 Environmental Health Perspectives 1027-1031 (2001). Crain DA, Guillette LJ Jr, Rooney AA, Pickford DB. Alterations in steroidogenesis in alligators (Alligator mississippiensis) exposed naturally and experimentally to environmental contaminants. 105 Environmental Health Perspectives 528-533 (1997).

cause feminization of males exposed during sexual development and maturation, and could also cause a hyper-estrogenic state in females. Potential health effects in humans could include birth defects of the penis, smaller genital size in males, decreased sperm production, behavioral changes, alterations in the time of onset of puberty, prostate inflammation, and breast cancer in females.

Dr. Hayes initially conducted research while under contract with Syngenta (formerly Novartis Crop Protection), but the published work was done independent of the company.[18] Syngenta has responded to the Hayes findings on males' laryngeal muscles in two ways: the company first submitted its own interpretation downplaying the importance of the Berkeley data, and then presented EPA with the results of a separate experiment by a new set of researchers that Syngenta hired to re-examine the effects of atrazine on laryngeal muscles. By contrast, it appears that Syngenta has completely ignored the research regarding gonadal abnormalities;[19] thus, these compelling results are unrebutted.[20]

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[18] *See* Press Release, *supra* note 15 (describing prior funding by Syngenta). Syngenta was formed in 2000 by the merger of Novartis and a company called Zeneca. Novartis itself was the product of a merger between two companies known as Ciba and Sandoz. *See* Syngenta, "Timeline/History," available online at http://www.syngenta.com/en/syngenta/time_prin.asp (visited April 10, 2002). For convenience, this notice refers to Syngenta and its predecessors as Syngenta.

[19] NRDC submitted Freedom of Information Act requests seeking any information that Syngenta may have submitted regarding the frog research, and also reviewed EPA's index of company reports of alleged adverse effects from atrazine, and could find no suggestion that the data regarding gonadal abnormalities has ever been reported.

[20] Recently, an organization calling itself the Triazine Network submitted a criticism of Dr. Hayes's preliminary results – that is, not the work published in *PNAS* – to EPA. *See* The Triazine Network, *The Significance of the Hayes et al. (2001) Study on the Current Understanding of Developmental Disorders in Amphibians Exposed to Atrazine* (April 12, 2002). This paper, released less than a week before Dr. Hayes's final study appeared in the peer-reviewed literature, should be given no credence whatsoever. It lacks credibility primarily because its main criticism – that the research had not been subject to rigorous peer review and publication, *id.* at 4, 5, 8 & 12-15 – is not valid now that Dr. Hayes has published his research in a prestigious, peer-reviewed journal. In addition, the paper's suggestion that Dr. Hayes's work on a non-indigenous species renders it inapplicable to the U.S., *id.* at 10, is belied by the fact that Dr. Hayes

Both Syngenta documents – the interpretation of the Berkeley data and the new experiment – are unconvincing (and un-peer reviewed) rebuttals to the published work. First, Syngenta's explanation of the Berkeley findings is paradoxical: the company concluded that "[t]here was no convincing evidence that atrazine increased the larynx cross-sectional area, *although statistically significant differences were noted. . .*" (emphasis added). It is also noteworthy that although Syngenta's report characterizes the Berkeley research for the company, there is no indication that Dr. Hayes or his colleagues were involved in the preparation of the company's analysis.

Syngenta's second submission to EPA – the company-funded re-study of effects on the male larynx muscle – also does not undermine the published research. The company claims that the new work was "more robust," in terms of "study design and statistical power" and states that it did not find a significant increase in laryngeal muscle size. Specifically, Syngenta alleges that the new study used a superior method of measuring the muscle's size.[21] These claims do not withstand scrutiny. For one, Syngenta's submission is an unpublished, non-peer-reviewed report. As such, it has received no independent expert review. Additionally, it is lacking in crucial detail that would allow for independent analysis; for example, it provides no information as to how

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and his colleagues have, as discussed above, found similar effects in resident wild frogs in atrazine-contaminated areas. Furthermore, the paper makes the preposterous criticism that Dr. Hayes fails to show a statistical correlation between the frog mating season and high atrazine levels, *id.* at 9-10; this claim ignores both common sense (frogs mate in the spring, and atrazine is applied in the spring) and the fact that Dr. Hayes found dramatic adverse effects in frogs at 0.1 ppb, a level found at all times of the year in many locations. Finally, the "Triazine Network's" criticisms suffer from precisely the fatal flaw that they incorrectly attribute to the Berkeley team's research: it is neither peer reviewed nor published, and obviously could not withstand such a rigorous process, as Dr. Hayes' studies have.

[21] Letter from Thomas Parshley, Senior Regulatory Manager, Syngenta, to James Tompkins, U.S. EPA (Jan. 15, 2001); Letter from Thomas Parshley, Senior Regulatory Manager, Syngenta, to Kathryn Bouve, U.S.

many animals were used, nor does it reveal the researchers' treatment methods. Such detail is critical because it is difficult to imagine how a second study, if performed appropriately, could find results contradictory to Dr. Hayes's findings, as the Berkeley work is unusually extensive and complete. Dr. Hayes's team examined one thousand histological sections taken from 100 frogs, to determine the anatomical region of the laryngeal muscle that consistently had the largest cross-sectional area. This area was then identified in each animal, and measured using a computer imaging program designed for such a purpose.[22]

The new Syngenta submission should not be given any weight. The researchers chose a method that seems designed to mask differences in laryngeal muscle size; in particular, they divided the measured cross-sectional area of the muscle by the body weight of the frog. This is a scientifically flawed methodology, because growth of the male frog laryngeal muscle is well-known to be dependent on androgen levels, and not on body size.[23] Even small males will grow normal male-sized laryngeal muscles, if their androgen levels are normal. This hormone-dependence is, of course, exactly why this particular male muscle can be used as an indicator of androgen levels.

EPA (Mar. 4, 2002). Note that, although the first letter suggests that it would address gonadal development issues, the Syngenta submission does not discuss the research identifying sexual abnormalities at all.

[22] Hayes et. al, *supra* note 12, at 5,477.

Prostate Cancer in Workers Exposed to Atrazine

On October 12, 2001, Syngenta submitted a report to EPA on cancer incidence among employees of its atrazine manufacturing facility in St. Gabriel, Louisiana.[24] Syngenta submitted this report only after NRDC and other citizens sought EPA's help in getting the information from the company.[25] When the new data arrived, they were shocking. Syngenta employees have markedly elevated incidence rates of prostate cancer. Several scientists, including one of the nation's leading epidemiologists at the National Cancer Institute, have reviewed the Syngenta report and determined that the statistically significant increase in prostate cancers among workers is a cause for concern.

At Syngenta's St. Gabriel facility, non-contract workers develop prostate cancer at a rate over three-and-a-half times higher than the Louisiana statewide average.[26] In addition, these cancers appeared commonly in younger workers (almost every cancer case was a man under age 55), and are most common in those workers who spent the most time at the facility. All but one of the observed prostate cancers in the entire cohort occurred in men with 10 years or more at the plant, and the company employees with prostate cancer worked an average of 20 years at the plant.[27] Although the company study did not include exposure histories of the workers, these figures suggest that the workers with the longest exposure history have the highest rate of cancer.

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[23] Fischer LM, Catz D, Kelley DB, nAndrogen-directed development of the Xenopus laevis larynx: control of androgen receptor expression and tissue differentiation, 170 Dev Biol 115-26 (July 1995).
[24] Delzell E, Sathiakumar N, MacLennan P. A Follow-Up Study of Cancer Incidence Among Workers in Triazine-Related Operations at the Novartis St. Gabriel Plant. Final Report. #455184-01 (Oct. 12, 2001) (hereinafter "Syngenta 2001 Report").
[25] *See* Letter from Erik Olson & Jon Devine, NRDC, to Stephen Johnson, EPA (June 25, 2001) (requesting EPA inquiry into ongoing prostate cancer research at St. Gabriel); Letter from Joseph McKernan, McKernan Law Firm, to OPP Docket 000637 (May 12, 2000) (same).
[26] Syngenta 2001 Report at p. 5 of 170.

The Syngenta report presents the data in a misleading manner that would not meet normal scientific standards in peer review.[28] First, the most glaring omission is that the company submission lacks any estimate of exposure history of the workers; it is remarkable – indeed, suspicious – for a company study to fail to include the exposures associated with specific job descriptions within the company, as this information would be crucial to determining whether the chemical exposure was the likely cause of workers' illnesses.[29] Second, more than 200 workers were excluded from the study because they were "known or presumed to have left Louisiana before 1988." This is a significant omission because these workers will have had the longest time since exposure, and therefore will be among those most likely to develop a work-related cancer (given that the latency period from exposure to disease onset may often be 15-20 years or more). Third, it appears that the company's study underestimated the potency of atrazine by including nearly 1,300 contract workers in the study population. Contract workers made up over 60 percent of the people examined, even though they only worked at the facility for a median of 1.4-2.5 years and were therefore far less likely to be at risk from chronic exposures; by adding marginally exposed individuals to the analysis, the company likely diluted the apparent frequency that exposed individuals develop cancer. Finally, the study does not

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[27] *Id.* at pp. 31 & 40 of 170.

[28] Letter from Dr. Aaron Blair, National Institutes of Health, to Dr. Jerome Blondell, U.S. Environmental Protection Agency, at 1 (Nov. 14, 2001) ("The major limitation of the study was the lack of detailed work histories on study subjects. *** [An] occupational study without such a component would not peer review anywhere.").

[29] Exposure misclassification is a well-known source of bias in epidemiological studies and is known to underestimate a chemical's disease-causing potential. Improved exposure assessment would likely reveal a more significant association between atrazine and cancer if the most exposed workers were clearly identified. The company's failure to provide this information is curious given the report's statement that "[d]etailed information on job title and work area was available for Novartis employees. . . ." Syngenta 2001 Report at p. 14 of 170.

consider the "healthy worker effect," well-known to epidemiologists, that worker studies tend to underestimate a chemical's harmfulness because workers, by and large, are more healthy than the population as a whole.[30]

Notwithstanding the fact that the analysis downplays atrazine's carcinogenicity, it is possible to extract relevant information from the reports to determine the rates of cancer among the exposed employees. The chart below presents NRDC's summary of the important statistics in Syngenta's report, which takes the crucial step of separating contract workers from employees to focus on the workers most likely to have significant exposures. This analysis shows exactly where the cancers are concentrated – in company employees who worked much longer on average – and thus suggests a dose-response relationship between atrazine and cancer, especially in combination with the fact that the company employees with prostate cancer had a median length of employment of 20 years at the end of 1997.[31]

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[30] Letter from Blair, *supra* note 28, at 1 ("The overall cancer excess [at St. Gabriel] is somewhat surprising because many retrospective cohort studies show a deficit of cancer overall because of the healthy worker effect."). Worker populations tend to be healthier than the general population because one ordinarily must be healthy to work. Accordingly, workers' disease and cancer rates tend to be lower than the average population. Thus, when an otherwise healthy worker population suffers cancer or disease rates above the general population, these may be considered suggestive of occupationally-related disease, even when the rates are not very elevated. *See, e.g.*, J. Baillargeon, Characteristics of the healthy worker effect, 16 Occup. Med. 359 (Apr.-June 2001); C.Y. Li & F.C. Sung, A review of the healthy worker effect in occupational epidemiology, 49 Occup. Med. (Lond) 225 (May 1999); H.M. Arrighi & I. Hertz-Picciotto, The evolving concept of the healthy worker survivor effect, 5 Epidemiology 189 (Mar. 1994); T. Wilcosky & S. Wing, The healthy worker effect. Selection of workers and work forces, 13 Scand. J. Work Environ. Health 70 (Feb. 1987).

[31] Syngenta 2001 Report at p. 40 of 170.

Prostate Cancers Among Atrazine Workers

	COMPANY EMPLOYEES	CONTRACT: PRODUCTION	CONTRACT: MAINTENANCE
Number of Workers	757	687	601
Median Age	46	40	38
Median Years Worked	10.6	1.4	2.5
Prostate Cancer Incidence (Observed/Expected)	14/3.9	1/0.8	2/2.0

Even faced with these figures, Syngenta refuses to blame atrazine, but instead the report attributes the dramatic excess in prostate cancer to the prostate-specific antigen (PSA) testing program operating at the facility. However, as discussed below, this explanation is speculative, could not fully account for the highly elevated number of cancers observed, and does not address the excesses in other cancer types, including bladder and blood cancers.

The company's report supposes that the increased cancer incidence is a result of more rigorous PSA screening among Syngenta employees than in the general public, and implies that atrazine is unlikely to be the cause of the cancers because many of the workers with cancer allegedly had low-exposure jobs. These claims lack factual support. Upon receiving Syngenta's report, EPA asked Dr. Aaron Blair, Chief of the Occupational Epidemiology Branch at the National Cancer Institute, to review the results, and he was quick to point out that the company made no effort to determine whether its exculpatory hypotheses were correct. For instance, Dr. Blair noted that one could determine how the incidence rates could be affected by improved screening, and that doing so would be

preferable to the company's approach of "simply stating that it might have an effect with no quantification of the magnitude." Likewise, Dr. Blair observed that the report's suggestion that a number of the victims were marginally exposed to atrazine was in tension with its claims that it lacked information on individual employees' actual exposures; in his words, "[i]f work histories were not available, how is it known that these cases worked in nonexposed jobs?"[32] Dr. Blair believes – contrary to the company's suggestions – that the data are compelling. He writes that "[t]he fact that there is an excess of prostate cancer and other cancers in the entire cohort," that is, considering people with varying degrees of exposure, "suggests that the relative risks may be even larger for subgroups with specific exposures."[33]

Even if the study is correct to suggest that improved screening may account for some increase in cancer incidence, the number of cancers at the St. Gabriel facility cannot

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[32] Moreover, the report's suggestion that eight of the victims worked in "areas that would have entailed sporadic, if any, exposure to atrazine," Syngenta 2001 Report at p. 41 of 170, is difficult to reconcile with the fact that employees "had to have worked in production, maintenance, laboratory or other jobs involving potential contact with triazines or precursor chemicals," *id.* at p. 14 of 170, in order to be included in the study.

[33] EPA also asked Dr. Edward Giovannucci to review the Syngenta-commissioned report, and he opined that the Syngenta report's suggestion in the study that the dramatic increase in cancers could be attributed to improved screening might be correct. Letter from Dr. Giovannucci to Jerome Blondell, U.S. EPA (Dec. 18, 2001). Dr Giovannucci's review is limited to an opinion on the influence of PSA screening on prostate cancer incidence, and does not provide a critique of the complete study, as was provided by Dr. Blair. Moreover, his short letter provides no quantitative estimate of the magnitude that PSA testing could be expected to bias incidence data, and overlooks the fact that the prostate cancers are mainly in those workers who also had the longest history of occupational exposure to atrazine. Dr. Giovannucci also mistakenly suggests that the data indicate that there was no relationship between the dose and prostate cancer -- this is inaccurate because the study provides no information about the amount of exposure each worker had. (Indeed, the fact that cancers are highest in workers with the longest exposure histories, suggests a dose-response relationship.) Finally, because Dr. Giovannucci's comments are limited to prostate cancer, he makes no assessment of the impact of an increase in other cancer types among long-term workers, which cannot be explained away by PSA screening (digestive system cancers, blood cancers, and others were elevated in long-term workers). NRDC Senior Scientist Dr. Jennifer Sass spoke with Dr. Giovannucci about his evaluation, and he stated that his review of the study was cursory, and fairly limited in scope. Most importantly, he stated that the study did not establish increased screening as the cause of the increased

be explained merely by rigorous testing. To evaluate the strength of the testing rationale, the most relevant data in Syngenta's report are those pertaining to "actively working" company employees, because only active workers were eligible for PSA tests.[34] Among company employees who were actively working at diagnosis, 11 had developed cancer, when 1.2 cases would be expected.[35] Taking these figures, and adjusting them to reflect the Syngenta report's suggestion that PSA screening may increase prostate cancer incidence by two to three-and-a-half times, one would expect only 2.4 to 4.2 cases rather than the 11 cases that occurred.[36] Even the adjusted difference between the number of observed cases and expected cases remains suggestive of carcinogenicity, especially considering the healthy worker effect.

Finally, the Syngenta report's attempt to blame better cancer testing for its cancer incidence rates ignores the fact that exposed workers developed other cancers for which the company was not testing. According to Syngenta's own report, "[t]he overall study group had more than expected cancers of the buccal cavity (3/2.1), esophagus (2/0.7), stomach (2/0.9), bladder (3/1.6), thyroid (2/0.6) and lymphohematopoetic system (7/4.5)." Dr. Blair remarked on these increases with interest, saying that "the PSA screening would not explain the excesses for the other cancers."

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incidence, and agreed that occupational exposures could contribute to the increased incidence of prostate cancer, in addition to other cancer types.

[34] *See* Syngenta 2001 Report at p. 6 of 170. In addition to the fact that the PSA testing program did not reach inactive employees, the Syngenta report's authors apparently did not attempt to find out whether many of these workers even had prostate cancer. *See id.* at p. 27 of 170 ("We did not attempt to identify prostate cancer cases among separated employees in 1998 or 1999, as [Louisiana Tumor Registry] data were not available for those years.").

[35] *Id.* at p. 37 of 170.

[36] Even assuming that improved PSA testing increases expected prostate cancer incidence rates by as many as six-and-a-half times, *see* 88 BJU International 811, 812 (2001) (finding 6.5 times increase in studied cohort), the resulting ratio would still be 11 observed cases to 7.8 expected cases.

Implications of the New Research

EPA recently completely disregarded epidemiologic studies linking atrazine to ovarian, prostate, testicular, and breast cancer, and to non-Hodgkin's lymphoma.[37] Although each of these studies, taken alone, had flaws, the weight of evidence suggested a potential human cancer risk that clearly should not have been ignored.[38] Dr. Hayes's groundbreaking work with atrazine-exposed frogs confirms that EPA's initial action was in error. Furthermore, the atrazine epidemiology results are consistent with the animal toxicology studies used as the basis for EPA's review. When both the human and the animal studies are considered, they form a very compelling picture for an association between atrazine and hormone-responsive cancer. Indeed, these studies involve precisely the kind of additional research that EPA's Scientific Advisory Panel (SAP) believed was missing when the SAP recommended downgrading atrazine's human carcinogenicity classification; the SAP stated at that time that "[t]he issue of atrazine and prostate cancer was briefly discussed but limited data were available for review. It was strongly recommended that EPA should review the data when it becomes available."[39]

Atrazine causes inflammation of the prostate in laboratory rats, alters testosterone metabolism, induces aromatase, and has other hormonal effects in the prostate.[40] Prostate cancers in humans, as in animals, could certainly result from hormone disruption. EPA

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[37] Solomon GM, NRDC. Comments on the Revised Preliminary Human Health Risk Assessment for Atrazine. Docket Control No. OPP-34237.

[38] Summarized in memorandum from RH Allen to R. Hawks Review of five atrazine epidemiology published articles for SAP. DP Barcode D262405. January 14, 2000.

[39] Scientific Advisory Panel, "Atrazine: Hazard and Dose-Repsonse Assessment and Characterization," SAP Report 2000-05, at 13 (2000), available online at http://www.epa.gov/scipoly/sap/2000/june27/finalatrazine.pdf (visited April 12, 2002).

should consider the elevated rates of prostate and other cancers in atrazine workers to be due to atrazine, as suggested by the Syngenta epidemiology study, and should take rapid action to address the risks to workers and to the general public.

Human Testing with Atrazine

In its human health assessment, EPA derived its estimate of how much atrazine penetrates exposed skin from the results of an experiment in which human subjects were intentionally exposed to the chemical. Because, as discussed below, the test in question was poorly designed and non-probative from a scientific standpoint, because the Agency's policy is not to use pesticide tests on humans while their propriety is under review, and because the human tests do not meet the principles of applicable law and ethics, including the Common Rule, 40 C.F.R. Part 26, the Nuremberg Code, and the Helsinki Declaration, EPA must correct its currently erroneous exposure estimates.[41]

Studies in rats indicate that approximately 22 percent of atrazine applied to the skin is absorbed. A study submitted by the registrant, however, dosed humans with atrazine and calculated a dermal absorption factor of only six percent. This study (MRID44152114) of 10 human "volunteers" was poorly designed, too small to have the

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[40] Simic B, Kniewald Z, Davies JE, Kniewald J. Reversibility of the inhibitory effect of atrazine and lindane on cytosol 5 alpha-dihydrotestosterone receptor complex formation in rat prostate, 46 Bulletin of Environmental Contamination & Toxicology, 92-99 (1999).

[41] In addition to the study discussed above, it appears that Syngenta has conducted at least one other human test of atrazine upon which it hopes EPA will rely. In comments to the SAP committee evaluating atrazine (document 7 in EPA docket OPP 00637), Syngenta submitted a document called "A Weight of the Evidence Evaluation of the Carcinogenic Potential of Atrazine Conducted According to USEPA's Draft Cancer Risk Assessment Guidelines," dated January 14, 2000. This document refers to a study in which atrazine was "administered orally to six male human volunteers," *id.* at p. 12 of 48 (citing two studies apparently submitted to EPA, with MRID numbers 43598603 and 43598604). Although the description of the studies is limited, the information about the size and demographics of the test group leads quickly to the conclusion that the results are scientifically useless and therefore disallowed under the principles discussed here. Accordingly, EPA must review the record of its atrazine decisions to date to ensure that this study did not affect its human health assessment in any way.

power to detect variability in the population, and too limited in scope to use. The study subjects were apparently exposed to a single topical dose of ^{14}C-atrazine at 6.7 (N=4) or 79 (N=6) ug/cm^2 for 24 hours. The experimenters made no attempt to account for conditions that could promote absorption, such as chapped or irritated skin, or for the conditions of vasodilatation that occur during showering or in hot weather. Furthermore, although the skin of infants and children is thinner and more permeable than the skin of adults, and is often moist with saliva, the experiment did not address such exposures. As these simple examples show, a sample size of ten adult males could not even begin to represent the range of natural variability within the population.[42]

In addition to the serious scientific flaws listed above, there are important ethical and legal concerns related to the practice of intentionally dosing human subjects with known poisons with no medical benefit to themselves in order to attempt to alter the assumptions in a regulatory risk assessment for the benefit of the pesticide industry. Such testing violates EPA's stated policy that it will not consider human tests in which people were intentionally dosed with toxic pesticides, breaks international and domestic law, and ignores the scientific and ethical advice provided to EPA by its scientific advisors, including:

1. The Nuremberg Code, which was adopted by U.S. judges in the wake of the Nuremberg "doctor trials" of Nazis after World War II. U.S. courts and others have relied on the code to establish minimum standards for human testing.[43]

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[42] This is particularly true regarding the population that EPA has been statutorily charged by the Food Quality Protection Act with protecting from aggregate exposure to atrazine: fetuses, infants, and children. *See* 21 U.S.C. 346a(b)(2)(C).

[43] *See Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10* ¶ 2 (Oct. 1946–April 1949) (requiring, among other things, that experiments on humans "be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study"), available online at http://www.ushmm.org/research/doctors/Nuremberg_Code.htm (visited May 9, 2002); *see also Grimes v. Kennedy Krieger Inst., Inc.*, 366 Md. 29, 99 (2001) ("The breach of obligations imposed on researchers by

2. The Helsinki Declaration, which as adopted by the World Medical Association, governs medical testing of human subjects, but also is used to judge the ethics of other human testing.[44]

3. The Common Rule, which establishes ethical and scientific rules for human testing. It was issued by HHS, and adopted by EPA in 1991.[45]

4. EPA Scientific Advisory Panel-Science Advisory Board majority report and accompanying minority report. The minority found that intentional human dosing with pesticides is always unethical. The majority said bad science is always unethical, and human testing is unethical if intended to weaken health protection, but could be ethical if intended to strengthen protection, subject to "rigorous to severe" ethical and scientific controls, and "active and aggressive scrutiny" by EPA.[46]

In particular, the dermal absorption study compromised these fundamental principles in the following ways:

1. The purpose of the experiment was *not* to improve health protection, but rather to reduce the estimated amount of atrazine absorbed by those exposed to it, and thereby to advance the interests of industry and agriculture. [Violates SAP-SAB Maj., Letter at 2 ¶d;]

2. There is no "reasonable likelihood" that the subpopulations serving as subjects would benefit from the study results. The study offered no benefit to subjects that we can discern. [Violates Helsinki, ¶B-19]

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the Nuremberg Code, might well support actions sounding in negligence in cases such as those at issue here."). An additional key principle of the Nuremberg Code is informed consent, *see* Code¶ 1 ("The voluntary consent of the human subject is absolutely essential."), and this requirement is echoed in FIFRA section 12(a)(2)(P), which prohibits any person from using "any pesticide in tests on human beings unless such human beings are (i) fully informed of the nature and purposes of the test and of any physical and mental health consequences which are reasonably foreseeable therefrom, and (ii) freely volunteer to participate in such tests). Although these elements are crucial, we do not presently have sufficient information to evaluate whether the atrazine human experiment satisfied these obligations; accordingly, they are not discussed further below.

[44] World Medical Association, Inc., "World Medical Association Declaration Of Helsinki," available online at http://www.wma.net/e/policy/17-c_e.html (visited April 12, 2002).

[45] *See* 45 C.F.R. part 46; 40 C.F.R. part 26.

[46] Science Advisory Board & Scientific Advisory Panel, "Comments on the Use of Data from the Testing of Human Subjects," EPA-SAB-EC-00-017 (Sept. 2000), available online at http://www.epa.gov/sab/ec0017.pdf (visited April 12, 2002).

3. The experiment does not "yield fruitful results for the good of society, unprocurable by other methods or means of study," because the study population was so miniscule as to be scientifically irrelevant, was not representative if the full population (including the relevant subpopulation of legal concern, infants and children), because the study would reduce protection, and because animal data already existed regarding the dermal absorption rate of atrazine. [Violates Nuremberg Code, ¶2]

4. The "[r]isks to subjects [are not] reasonable in relation to the anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected," since there was neither a benefit to subjects, nor important "expected knowledge." [Violates Common Rule § 46.111(a)(2)]

5. The study does not yield scientifically and statistically valid, relevant data. The sample size was too low to produce results of statistical validity, and infants and children were not represented, and could not be represented, in the study. "Bad science is always unethical; research protocols that are fundamentally flawed, such as those with sample sizes inadequate to support reasonable inferences about the matter in question, are unjustifiable." [Violates SAP-SAB Majority, Letter at 2¶c]

6. The report insists on the secrecy of its results except under limited circumstances, contrary to requirements that results of human studies are to be published or disseminated. The report states that the "data are the property of the Ciba Crop Protection Division of Ciba-Geigy Corporation, and as such are considered to be confidential for all purposes other than compliance with FIFRA Section 10." This is contrary to the requirement that for human studies, "[n]egative as well as positive results should be published or otherwise publicly available." [Helsinki ¶B-27]

Faced with objections to human testing of pesticides, the Agency has requested that the National Academy of Sciences conduct a review of the scientific and ethical issues posed by use of these studies.[47] The Agency has stated that, "[d]uring the Academy's consideration of the issues and until a policy is in place, the Agency will not

[47] Letter from Stephen Johnson, Assstant Administrator, EPA to National Academy of Sciences. December 14, 2001. Available online at www.epa.gov/epahome/headline3_121401.htm (visited April 12, 2002).

consider or rely on any such human studies in its regulatory decision making, whether previously or newly submitted."[48]

In order to follow the law, science, good conscience, and its own policy, EPA must reject the human study used to derive atrazine's dermal absorption factor. Accordingly, the Agency must re-calculate atrazine exposure using the 22 percent penetration factor established in other research.

Hazardous Exposures Are Unnecessary

In light of the health evidence discussed above, perhaps the most appalling aspect of EPA's continued licensing of atrazine is the fact that crops can be profitably produced without using this toxic chemical at all, or with dramatic reductions in its use. This is so because modern cultivation and herbicide use practices have evolved well beyond broadcast spraying of herbicides such as atrazine. Under the FFDCA, once EPA finds that aggregate exposure to pesticides is not safe (as it must in light of the evidence discussed above), EPA must revoke atrazine's tolerances without having to consider the availability of alternatives. However, in this case it is clear that such alternatives are readily available.

On working, non-organic farms in Iowa, farmers found that they could plant their corn crops in elevated ridges, and remove weeds from those ridges mechanically, increasing their profitability and eliminating the need for atrazine use. This practice, known as "ridge till," is a win-win solution for farmers who care about the environment. When a crop is ready to be planted, the farmer simply shears off the top part of the ridge,

[48] EPA newsroom. December 14, 2001. Available online at http://yosemite.epa.gov/opa/admpress.nsf/b1ab9f485b098972852562e7004dc686/c232a45f5473717085256b2200740ad4?OpenDocument (visited

thereby removing between 80 and 100 percent of the weed seeds. Ridge tillage obviates the need to apply poisons such as atrazine to prevent weed growth, and the money farmers save by cutting out herbicides more than outweighs the additional labor costs involved in ridge tillage.[49] Similarly, farmers can plant their crops in narrowly-spaced rows, which has the effect of choking out weeds naturally.[50] Still another option is to add a third crop to the traditional corn-soybean rotation, a practice which makes it harder for weeds that thrive amongst any one species of crop to persist over time. Work in Iowa comparing conventional corn/soybean rotation with a reduced chemical corn/oat/meadow rotation found that the low-chemical option cut production costs by half. Net returns were similar between the two systems.[51]

Even less ambitious weed control options can cut atrazine use dramatically. It is well-accepted that herbicides can be effective at rates below those indicated on the label,[52] and it is axiomatic that using less atrazine means less atrazine-polluted water bodies. Likewise, "spot spraying" of herbicides in locations where weeds are worst can make significant reductions in the amount applied.[53] Finally, albeit less desirable from a

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April 12, 2002).

[49] Practical Farmers of Iowa, "Weed Management in Ridge Tillage," available online at http://www.pfi.iastate.edu/OFR/RT_weeds.htm (visited April 12, 2002); Natural Resources Defense Council, "Harvest of Hope," at 87 (1991).

[50] Iowa State University, "Pest Management in Iowa: Planning for the Future," at 68 (June 1996). A similar effect can be accomplished by planting in well-spaced rows – which provides farmers better access to their crops – in which the crops are densely packed within the rows themselves.

[51] Natural Resources Defense Council, "Fields of Change: A New Crop of American Farmers Finds Alternatives to Pesticides," at 27 (July 1998); Harvest of Hope at 85-86. Rotating crops alone can reduce pesticide use 10-50%. The ordinary pattern of rotating between corn and soybeans is not effective; these crops have similar weed pressures. Iowa State University, "Eight Ways to Reduce Pesticide Use," at 20 (June 1999).

[52] Planning for the Future, *supra* note 50, at 67 (June 1996) (noting equivalent effectiveness for use rates between 25 and 50 percent below label).

[53] Eight Ways to Reduce Pesticide Use, *supra* note 51, at 22 (estimating 10 to 25 percent reduction in herbicide use).

public health and environmental standpoint than these improved cultivation techniques, there are of course chemical alternatives to atrazine that do not cause widespread drinking water contamination.

Conclusion

EPA's current working human health assessment of atrazine is fatally flawed. Dr. Hayes's research indicates that atrazine causes harm through a mechanism of action that the Agency has ignored to date, Syngenta's own study suggests a causal link between atrazine and prostate cancer, and EPA mistakenly underestimated exposure to the chemical in reliance on a dubious and unlawful experiment dosing humans with atrazine. Moreover, available information about farming techniques reveals that there are dramatic reductions that can be made in the current rates of atrazine use, making these dangerous exposures all the more unreasonable. The Agency must correct these grave errors in advance of its Interim Reregistration Eligibility Decision for atrazine.

Beyond improving its risk assessment, however, EPA must revoke all tolerances under FFDCA § 408 for atrazine in light of:

- widespread exposure of hundreds of thousands of Americans to drinking water at levels in excess of EPA's drinking water standard;[54]
- the accumulating mountain of evidence that atrazine poses greater serious risks of endocrine disruption;[55]

[54] *See* notes 1-5, *supra*, and accompanying text.
[55] *See* notes 9-17, *supra*, and accompanying text.

- the likelihood that atrazine causes cancer in exposed people, and Congress's admonishment in passing the Food Quality Protection Act that tolerances may not permit a greater than a one-in-one-million cancer risk.[56]

Therefore, because aggregate exposure to atrazine is not "safe" under the terms of FFDCA § 408, and because its health and ecological effects pose unreasonable adverse effects on the environment, EPA also must cancel atrazine under FIFRA §§2(bb) & 6.

[56] *See* notes 6-8 & 24-36, *supra*, and accompanying text; *see also* H. Rep. 104-669, 104th Cong., 2d Sess. (July 23, 1996) (For harms "such as a cancer effect, the Committee expects, based on its understanding of current EPA practice, that a tolerance will be considered to provide a 'reasonable certainty of no harm' if any increase in lifetime risk, based on quantitative risk assessment using conservative assumptions, will be no greater than 'negligible.' It is the Committee's understanding that, under current EPA practice, . . . EPA interprets a negligible risk to be a one-in-a-million lifetime risk. The Committee expects the Administrator to continue to follow this interpretation.").