UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES (OPPTS)

JUL - 7 2005

Ms. Julia Govis
4378 Eldamain Road
Plano, Illinois 60545

RE: Request for Correction on EPA's Atrazine Reregistration Activities (RFC # 05001)

Dear Ms. Govis:

This letter is in response to your e-mail dated January 10, 2005, and received by the Environmental Protection Agency (EPA) on January 12, 2005. For referencing purposes, your submission has been assigned EPA IQG # 05001, and is posted on the IQG Web site at http://epa.gov/quality/informationguidelines/iqg-list.html#05001. We regret the delay in responding to your request.

In your e-mail, you indicated that you were filing a request for correction under EPA's Information Quality Guidelines (IQGs) because you were concerned with the Agency's reregistration activities related to the pesticide atrazine. Specifically, you wrote that you had new information for EPA to consider and that you were unable to provide previously because you were unaware of the Agency's activities or previous opportunities to submit comments. You expressed concern about the atrazine review process, data used, and outcome of the Agency's activities.

EPA is responsible for registering pesticides intended for sale, distribution and use in the United States, and for setting the pesticide's tolerance or maximum residue levels allowed to remain in or on foods and animal feed. Under the reregistration program, the Agency is conducting an aggressive program to review older pesticides (pesticides first registered before November 1984) to ensure that they meet current safety standards for the protection of human health and the environment. In 1996, the Food Quality Protection Act (FQPA) made major changes to the way in which EPA makes its regulatory decisions and requires that EPA review the safety of all existing tolerances that were in effect as of August 1996. Tolerance reassessment is being accomplished through the pesticide reregistration program.

It is important to first note that the Office of Management and Budget and EPA IQGs provide for *correction of disseminated information*, and do not provide for the *correction of administrative processes*. Nevertheless, I can assure you that the Agency's goals are to conduct reregistration and reassessment activities in an open and transparent manner, to give the public ample opportunities to participate, and to ensure all regulatory decisions are based on sound science. To achieve these goals, the Agency has established a robust process for reregistration activities, including external scientific reviews, several opportunities for public

involvement, and the use of a public docket to facilitate access to the information related to a particular pesticide under review. The Agency is using this process to review atrazine. We feel confident that the policies and procedures in place at EPA are consistent with the quality principles described in our IQGs for disseminating information to the public.

I have enclosed a brief summary of the Agency's activities with regard to our review of atrazine, along with several Web site links for additional information about atrazine and the pesticide reregistration program. In addition, to provide a more detailed description of EPA's science-based public process for regulating pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), enclosed is a copy of the Agency's written statement before the Agriculture and Rural Development Committee of the Minnesota House of Representatives, dated February 16, 2005. This statement also specifically addresses concerns, similar to those you expressed, that were raised by this Committee about EPA's evaluation of atrazine.

EPA's IQGs describe what should be included by persons submitting a request for correction of information (Section 8.2 of the Guidelines). One of the items that should be included is a specific citation of the information that the person believes should be corrected. While you expressed concern about the process and data used by EPA, your email did not reference specific information that should be corrected, nor did it provide new information for the Agency's consideration. After carefully reviewing your email, EPA has determined that the information disseminated in the context of the Agency's reregistration activities related to the pesticide atrazine does not warrant correction under the IQGs.

Nevertheless, we share your concerns about protecting humans, wildlife, and the environment from the adverse effects of pesticides. We are taking steps to ensure that use of atrazine does not pose unreasonable risks. I hope this letter and the enclosed information clarify EPA's activities with regard to the Agency's review of atrazine and the Agency's IQG program. If you have any further questions or concerns about atrazine, please feel free to contact the chemical review manager for atrazine, Diane Sherman at 703-308-0128.

Sincerely,

Susan B. Hazen
Principal Deputy Assistant Administrator

Enclosures

Summary of Atrazine Reregistration Activities

The following is a brief summary of the Agency's activities related to its review of the pesticide atrazine. EPA has also prepared a factsheet/Q&A document that is available at http://www.epa.gov/pesticides/factsheets/atrazine.htm. The factsheet/Q&A document provides both general and technical information about atrazine and its current regulatory status under pesticide and water environmental laws.

Atrazine, an herbicide, is primarily used to control pests such as broadleaf and some grassy weeds for a variety of major and minor agricultural crops as well as some non-agricultural uses. Atrazine is being reviewed by EPA's Office of Pesticide Programs as part of EPA's ongoing program to reevaluate, or "reregister", older pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The purpose of this reregistration program is to ensure that the older pesticides meet current health and environmental safety standards, including the health-protective measures called for in the Food Quality Protection Act of 1996 (FQPA). During the reregistration process, a risk assessment is performed in which EPA considers potential risks to human health and the environment from the use of the pesticide. Where we find that a pesticide does not meet these current safety standards, EPA may impose new restrictions on its use or ban it entirely. EPA's evaluation of atrazine is based on a thorough review of an extensive body of the best available scientific data and studies and has been the subject of public and stakeholder participation, including independent scientific peer review. EPA's final reregistration decision on atrazine will reflect a careful and rigorous scientific assessment of the potential risks associated with its use.

Data to support EPA risk assessment, reregistration, and tolerance reassessment decisions comes from a variety of sources (e.g., scientific studies and the public) and is reviewed and substantiated by a variety of experts (e.g., scientific panels and peer reviewers). Under FIFRA, Congress has placed the burden of proving safety on the companies that want to make and sell pesticide products. Thus, the pesticide companies, rather than the taxpayers, shoulder the costs of performing safety studies on pesticides required by EPA. The pesticide companies submit studies to EPA for review, and the Agency uses these and other scientific data to develop detailed risk assessments for every use of each pesticide. Further, pesticides companies are required by FIFRA to report all information relating to the potential adverse effects of their products on human health and the environment. Academia and interest group researchers offer additional sources of scientific data to support risk assessment decisions. We review scientific work from all sources, but we do not automatically accept the scientific conclusions. To assist in this review, EPA has issued both guidelines that provide instruction about how to conduct different types of studies and Good Laboratory Practice (GLP) regulations that describe, for all types of laboratory research, the minimum procedures to ensure high quality data. The Agency reaches its risk assessment, reregistration, and tolerance reassessment decisions through a systematic, objective evaluation of all relevant data and information. Each step of the process uses scientifically peer-reviewed, documented procedures.

EPA's peer review process (as documented in EPA's Peer Review Handbook – 2nd Edition at http://www.epa.gov/osa/spc/htm/2peerrev.htm) provides an additional layer of analysis for data and preliminary decisions. Peer reviewers undergo a rigorous review and selection process to ensure they do not have conflicts of interest or bias with regard to their review of the science. Further, our peer review process allows a variety of scientists to participate in peer review – EPA scientists, other government agency scientists, and non-governmental scientists from the public. Data to support the atrazine reregistration was peer reviewed by the FIFRA Scientific Advisory Panel (SAP) in 2000 and 2003. Additional information about the FIFRA SAP can be found at http://www.epa.gov/oscpmont/sap/.

The Agency makes great efforts to engage the general public and other interested stakeholders during the reregistration review process. To date, there have been four public comment periods in which any interested party has been able to provide EPA information about the uses of atrazine, the potential risks, and the mitigation of those risks. EPA highly values these public comment periods because they

are an extremely important part of the reregistration review process and because they often provide critical information that can be considered along with the scientific data when the Agency makes its reregistration decision. We use data that are submitted to us or otherwise available to us – including data that are provided by companies and anyone else. However, for us to be able to use the data in our decision making processes, the data must meet certain standards of acceptability – these standards are mirrored in our Information Quality Guidelines. Further, all public comments that are submitted in a proper and timely fashion become part of the official public record. Keeping in mind that atrazine is estimated to be the most heavily used herbicide in the United States, a large number of interested parties submitted information on the issues and presented a diversity of arguments in support of their respective positions.

After carefully collecting and considering all of the available information and data on atrazine and upon completion of the peer review process, EPA issued its Interim Reregistration Eligibility Decision (IRED) for atrazine in January 2003. Subsequently, EPA issued a revised IRED in October 2003. The Final Reregistration Eligibility Decision (Final RED) and tolerance reassessment decision for atrazine will be issued once EPA completes a comprehensive risk assessment for all of the triazine herbicides, a category of pesticides of which atrazine is a member. As documented in the atrazine risk assessment and the revised IRED, EPA believes that atrazine is not likely to cause cancer in humans based on the available information. However, the Agency plans to review several ongoing studies as they are completed and, as needed, will consult the FIFRA Scientific Advisory Panel, which is comprised of non-EPA scientific experts. EPA's current findings and future plans regarding the question of carcinogenicity are further detailed in the October 2003 revised IRED. The IRED documents, as well as many other documents addressing atrazine that you may find useful, can be found at http://www.epa.gov/oppsrrd1/reregistration/atrazine.

Despite the fact that we have not yet completed our review of atrazine, we are taking proactive steps to protect human health and the environment from risks posed by the use of atrazine. EPA is implementing an extensive drinking water monitoring program as well as an ecological monitoring of watersheds where atrazine is used. If necessary, based on the results of this monitoring, further steps to manage risks for atrazine may be taken, including removal of atrazine use in geographic areas of concern.

There are additional ways of finding information on atrazine as well as other EPA pesticide activities. In addition to atrazine's IRED documents mentioned above, you may be interested in other extensive information the Agency has posted on the internet about atrazine. Please visit: http://www.epa.gov/oppsrrd1/reregistration/atrazine.

If you are interested in other EPA pesticide activities, please visit: http://www.epa.gov/pesticides. You can also subscribe to the Office of Pesticide Program's e-mail "listserve" at: http://www.epa.gov/oppfead1/cb/csb_page/form/form.html. Twice a week, subscribers to this listserve will receive e-mail updates on recent regulatory decisions, press announcements, and other information of interest from the Office of Pesticide Programs. This listserve is for all pesticide information – it is not just limited to information on atrazine.

Statement of Anne E. Lindsay

Deputy Director, Office of Pesticide Programs
U. S. Environmental Protection Agency

before the

Agriculture and Rural Development Committee
of the
Minnesota House of Representatives

February 16, 2005

My name is Anne Lindsay; I serve as the Deputy Director of the Office of Pesticide Programs (OPP) at the US Environmental Protection Agency (EPA or Agency). I appreciate the opportunity to testify before the Agriculture and Rural Development Committee of the Minnesota House of Representatives. I will describe the EPA's science-based public process for regulating pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and will also specifically address concerns about EPA's evaluation of the pesticide, atrazine, a widely-used herbicide.

EPA has a very highly regarded program for evaluating pesticide safety and making regulatory decisions. EPA's reputation rests on our world-renowned expertise in pesticide risk assessment. Our approach to decision-making is widely considered to be a model for transparency and openness. Using this approach, the Agency makes decisions consistent with scientific information and protective of public health and the environment.

Unfortunately, certain mischaracterizations of our regulatory process – particularly with respect to atrazine – are circulating in a variety of public venues. These mischaracterizations call into question the scientific soundness and the integrity of our work. Since public confidence is essential to the effectiveness of any regulatory program, EPA welcomes the opportunity to correct the record.

The Agency has carefully evaluated the available data, including research reporting that very low levels of exposure to atrazine harm frogs. We have also considered whether this research has implications for human health. But, before addressing the controversy over atrazine's impact on amphibian species, let me review how EPA regulates pesticides, so you can understand our position in the context of EPA's long history of environmental protection.

<u>EPA's Program for Regulating Pesticides</u>

EPA's Office of Pesticide Programs (OPP) is charged with administering FIFRA, under which we must ensure that use of a pesticide does not cause "unreasonable adverse effects on the environment." This safety standard requires EPA to consider not only the potential harm to human health and the environment from using a pesticide, but also the benefits of its use. The Agency has broad authority to restrict the way a pesticide may be used in order to lower its risks, and EPA may allow use of the pesticide only if we think the benefits outweigh the remaining risks.

The pesticide program includes two major components: registration (the licensing program that reviews new pesticide products before they are allowed into the marketplace) and reregistration (the program that reexamines previously approved pesticides against current-day scientific and safety standards). EPA is actively reviewing atrazine as part of its reregistration program, and is statutorily required to reach a decision on atrazine by August 3, 2006. Through our product-by-product licensing decisions in the registration and reregistration programs, EPA determines the restrictions under which we will allow sale and use of a pesticide. These restrictions appear in the form of use directions on the labeling of each pesticide product. It is a violation of federal law to use a pesticide in a manner inconsistent with its labeling. State lead agencies, like the Minnesota Department of Agriculture, enforce proper use of pesticides.

Both the registration and reregistration programs for evaluating the safety of pesticides rest on the same two fundamental principles: basing decisions on sound science and making our decisions through a process that is transparent and open to everyone.

Sound Science.

Under FIFRA, Congress has placed the burden of proving safety on the companies that want to make and sell pesticide products. Thus, the pesticide companies, rather than the taxpayers, shoulder the cost of performing the safety studies on pesticides required by EPA. Consistent with this design, EPA has promulgated regulations establishing a rigorous battery of tests necessary to support the registration of a pesticide. A typical agricultural pesticide must undergo over 100 different tests, which can cost in excess of $12 million, to characterize its potential to harm humans, wildlife, plants, and to evaluate its fate and movement in the environment. The pesticide companies submit these studies to EPA for review, and the Agency uses these and other scientific data to develop detailed risk assessments for every use of each pesticide. In the event that a test is not scientifically sound or EPA simply needs more information, EPA may require a company to conduct additional studies. Further, because of the critical role that scientific data play in EPA decision-making, registrants are required by FIFRA to report all information relating to the potential adverse effects of their products on human health or the environment, for example, the results of new research a registrant learns about or performs.

EPA holds itself accountable to the public for ensuring the quality of its scientific risk assessments. We review scientific work from all sources, but we do not automatically accept the scientific conclusions of anyone else – whether they are industry, academic, or interest group

researchers. Rather, EPA reaches its conclusions through a systematic, objective evaluation of all relevant information. Each step of the process uses scientifically peer-reviewed, documented procedures.

EPA always starts with the scientific data. We look at all available information from every source – whether from pesticide companies, other governments, or the published literature. We look closely at every study to determine whether the results are scientifically sound, that is, whether the testing methodology followed standard scientific procedures and data are consistent with the reported methodology. To assist in this review, EPA has issued both guidelines that provide instruction about how to conduct different types of studies and Good Laboratory Practice (GLP) regulations that describe, for all types of laboratory research, the minimum procedures to ensure high quality data. In addition, we have record retention requirements under which all documents relating to studies performed for pesticide registration must be maintained for the life of the registration. These guidance documents are complemented by a laboratory inspection program that monitors testing facilities for GLP compliance. Finally, we have issued guidance documents that specify how the results of a study should be reported to EPA. This guidance ensures that EPA receives all of the relevant information about a test in a format that is easy to evaluate. If we have any questions about the integrity of a study, we review the underlying raw data, going back to the test facility to inspect lab notebooks if necessary.

When EPA reviews a study, we follow published, peer-reviewed Standard Evaluation Procedures. These internal guidance documents instruct the Agency's scientific reviewers on what types of information to look for and how to analyze the data. The reviewer always double checks all of the analysis reported by the study sponsor. EPA also compares the results from one test with data from other studies to detect possible inconsistencies. It is not unusual that EPA will disagree with the conclusions reached by an individual researcher. At the end of the review, the scientist documents the review in a Data Evaluation Report (DER).

EPA uses peer-reviewed procedures to analyze data to produce risk assessments. For example, EPA follows the framework set out in the Agency-wide Ecological Risk Assessment Guidelines (EPA 1998) when assessing potential for a pesticide to cause adverse effects on the environment. The basic approach to ecological risk assessment has two components, a hazard evaluation and an exposure estimate. Toxicity studies in multiple species generate data that permit EPA to determine levels for both short-term and long-term exposures which would be unlikely to harm wildlife and plants. EPA then compares these hazard benchmarks to estimates of the amount of pesticide expected to occur in the environment from use of the product. EPA calculates exposure estimates using peer-reviewed models and scientific data on the persistence and mobility of each pesticide. The models employ data in such a way that the resulting estimates are likely to overestimate the amounts of pesticide exposure that wildlife and plants will likely receive. EPA then compares the toxicity of the pesticide with the expected environmental exposure to assess whether there is a potential risk, and if so, whether EPA needs to consider regulatory measures to mitigate that risk.

Because scientific studies are complex and sometimes the results do not agree, the interpretation of data involves considerable scientific care and judgment. EPA considers both multiple lines of evidence and, within a single line, uses a "weight of evidence" approach. By multiple lines of evidence, we mean that we look at different kinds of information – for example various types of laboratory studies, field incident reports, and the behavior of similar chemicals. Within a line of evidence we may have multiple data sets; when they do not agree, we examine each study and make a judgment based on the "weight of evidence." The Agency does not tally the number of studies yielding a particular result and simply rely on the outcome with the largest number of studies. Instead, the weight of evidence judgment involves evaluating the quality and robustness of each individual study, giving greater weight to better run studies, and then looking across all of the studies to decide what the preponderance of the data shows.

To ensure we reach the best possible conclusions, both the reviews of individual studies and risk assessments undergo scientific peer review to assure that scientific issues are handled consistently and that the analysis is carefully documented. EPA has longstanding internal peer review processes consistent with the Agency's Peer Review Guidance (2000), which it uses for all of its assessments. In addition, when we encounter a significant scientific controversy, we seek independent, external, expert scientific peer review. Sometimes we will work with scientists in other federal agencies, but on the most important issues we turn to the FIFRA Scientific Advisory Panel (SAP). Specifically created by Congress, the SAP is a federal advisory committee subject to the requirements of the Federal Advisory Committee Act (FACA). As such, it must comply with requirements for balance, objectivity, openness, and transparency. The Government Accounting Office has evaluated the SAP, along with many other scientific peer review groups, and concluded that the SAP is one of the best in the business. (See Report GAO-04-328: "Federal Advisory Committees – Additional Guidance Could Help Agencies Better Ensure Independence and Balance" (2004).) The Office of Government Ethics has also reviewed and commended highly the operations of the SAP.

An Open and Transparent Process.

EPA also believes in the importance of an open and transparent process. By "open" we mean that everyone, at any time, can provide information for our consideration, and everyone has the opportunity to comment on both our proposed decisions and the reasons for them. Of course, to make the comment opportunities meaningful, our process must be transparent. By "transparent" we mean that all of the data and analytical information we have considered, as well as the way in which we use the data to reach decisions, are available to the fullest extent permitted by law.

In our reregistration program, we typically follow a structured public participation process that provides several opportunities for comment. After giving registrants of a pesticide a short opportunity to correct errors in our draft risk assessment, EPA issues a preliminary risk assessment for public comment. This assessment contains our conclusions about the extent of potential risk to public health and the environment; EPA also makes available, on request, our written reviews of every scientific study on which we relied. After the close of the comment

period, we carefully review all new information, as well as each public comment. We prepare a written response to comments and, as necessary, a revised risk assessment, and again invite public comment on these documents and solicit comment on what measures are needed to address any risk concerns. Throughout this process, we may also hold public meetings for interested stakeholders to explain our risk assessments and regulatory decisions and to hear their comments and reactions. Finally, we issue a Registration Eligibility Determination (RED). This document contains our final risk assessment and conclusions regarding whether the pesticide meets the statutory standard for reregistration, and if not, what regulatory measures would be necessary to mitigate identified risks. (When the pesticide is part of a group of chemicals that EPA is reviewing because the group shares a common mechanism of toxicity, EPA issues an Interim RED (IRED). Once EPA completes its risk assessment of the common mechanism group, the Agency updates its decision and issues a RED.)

EPA's History of Environmental Protection

In addition to the numerous regulatory actions we have taken under FIFRA to protect human health, EPA has banned or severely restricted numerous pesticides over the years because they pose serious risks to the environment. In fact, one of the most visible and memorable actions by EPA happened in the Agency's early years when we completed the work started by USDA to ban DDT. This required extended hearings at EPA and ultimately judicial review by the second highest court in the nation. Since then, we have also banned a number of other pesticides including benomyl, ethion, ethyl parathion, fenthion, sodium fluoroacetate, strychnine, and thallium sulfate, and refused to register chlorfenapyr for use on cotton. We have severely restricted the uses of dozens of other pesticides including aldicarb, azinphos methyl, carbofuran, chlorpyrifos, diazinon, dicofol, methyl parathion, naled, and thiophanate methyl.

Atrazine

Atrazine is one of the most closely examined pesticides in the marketplace. Atrazine was first registered in 1958, a time when the requirements for registration were not as strict as they are today. Over the intervening 47 years, there have been a range of human health and environmental concerns raised about this pesticide. EPA has independently examined these concerns and responded in a variety of ways, depending on what the data showed us about risk, resulting in changes in use patterns, monitoring triggers, and requirements for new data. Where appropriate, EPA has consulted external experts. In addition to the multi-stage public comment process that is a standard part of our reregistration program, EPA has provided many additional opportunities for public participation on atrazine, as it has conducted its reviews of the scientific issues relating to cancer and to potential effects on frogs.

Although EPA has examined aspects of the atrazine registration in the years following 1958, EPA began its comprehensive reevaluation of atrazine for reregistration in 2000. There are nearly 6,000 studies in EPA files on the human health and environmental effects of atrazine. We developed a preliminary risk assessment and took public comment on it in 2001. After reviewing public comments, we issued a revised risk assessment for public comment in 2002.

We developed a statement of the Agency's regulatory position and made that public in an Interim Reregistration Eligibility Determination document in January 2003. (EPA issued an "interim" RED because we intend to assess the cumulative effects on human health of exposure to atrazine and two other chemically similar pesticides, simazine and propazine.) The IRED required extensive drinking water monitoring in Community Water Systems where atrazine levels had exceeded our level of concern; reduced the maximum application rate for liquid formulations on lawns and turf; and required more stringent personal protective equipment and engineering controls for some workers.

Because we had received and evaluated new information, we issued a revised IRED in October 2003. The revised IRED required ecological monitoring programs in surface water bodies and required studies on amphibians to investigate potential effects of atrazine on endocrine systems. At all of these steps, EPA has been fully transparent and every segment of the stakeholder community has had the chance to participate fully. We expect to conclude our reregistration review of atrazine by August 2006, and to incorporate into our decision the results of the ongoing amphibian toxicity studies, as well as our assessment of any other new data developed on atrazine.

Atrazine and Cancer

In recent years, scientific data on atrazine has raised several particularly difficult issues, and EPA has taken special measures to air those issues fully before reaching a final position. The debate over whether atrazine might cause cancer is an example. In 2000, after reviewing various rat studies in which atrazine produced tumors, EPA asked the SAP to review our determination that atrazine was a potential human carcinogen. The SAP disagreed with our conclusion, saying that on the basis of the available human epidemiology studies and multiple types of tests in laboratory animals, atrazine would affect humans differently from rats. Therefore the SAP did not expect atrazine to act as a human carcinogen. After careful analysis, we were persuaded by the SAP and accordingly revised our risk assessment to reflect the conclusions of the SAP.

The subject of carcinogenicity was not settled, however, because in 2001, the registrant, Syngenta Inc., informed EPA, under FIFRA's adverse effects reporting requirement, that a study of workers in their manufacturing plant in Louisiana showed an elevated level of prostate cancer. Syngenta claimed that the higher number of prostate cancer cases was due to the company's health program that resulted in virtually every worker at the plant undergoing screening for prostate cancer – a rate of screening much higher than is common in the general population of workers. EPA reviewed these data and then, because of the difficulty in interpreting the data, sought external peer review. Finally, EPA presented these data to the SAP for a review in July 2003. In addition to the Syngenta worker data, EPA also provided the SAP with the results from the Agricultural Health Study, which showed no association between atrazine and prostate cancer. (The AHS, conducted by the National Institute of Health with support from EPA and others, is the largest study of pesticides and cancer ever performed; it has nearly 90,000 pesticide users and spouses, many times the several hundred workers in Syngenta's

manufacturing facility.) The SAP agreed that some or all of the apparent increase in prostate cancer was due to intensive health screening programs, but the SAP indicated that additional analysis of the Louisiana data was needed and that Syngenta should continue to follow the workers in coming years. Syngenta has conducted the additional analysis and is continuing to monitor its workers. In addition, the AHS and other epidemiological research should produce new data on the potential carcinogenicity of atrazine in the coming years, and we have committed to analyzing all of this information and bringing the new results, as well as all previous research, to the SAP for another review.

Atrazine's Effects on Amphibians

The Agency has used a similar approach to resolving the controversy over whether atrazine harms frogs. EPA has taken an especially close look at the research conducted by Dr. Tyrone Hayes' research which reports that atrazine adversely affects sexual development in frogs, causing a mixture of sex organs in a single animal. EPA has concluded that the existing data are insufficient to demonstrate that atrazine causes such effects. The Agency's conclusions are supported by the independent, expert peer review of the SAP.

Dr. Hayes published the first report on his scientific research in 2002. In 2003, EPA began to collect all scientific studies that examined the potential effects of atrazine on various species of frogs, including all of the studies published by Dr. Hayes. (As part of its efforts to understand the available data, EPA scientists visited Dr. Hayes' lab and reviewed some of his raw data.) Altogether, EPA evaluated 17 different laboratory and field studies, including 4 studies authored by Dr. Hayes. The Agency used this information to prepare a 95 page "White Paper on Potential Developmental Effects of Atrazine on Amphibians" (White Paper) supported by over 35 references.

EPA's publicly available White Paper found that all of the available information was scientifically flawed. Because of these flaws, no firm conclusions could be drawn about whether atrazine affects frogs and if so, at what levels. In effect, all of the 17 amphibian studies with atrazine contained significant methodological flaws that severely limited the utility of each specific study in determining the potential effects of atrazine on sexual development in frogs. None of the laboratory studies on atrazine – whether performed by laboratories under contract with Syngenta, or performed by Dr. Hayes or others – were conducted in accordance with the standard ASTM International (formerly known as the American Society for Testing & Materials) protocols. These protocols were developed by the scientific community and published by ASTM over 20 years ago, to provide guidance on the proper way to conduct basic aquatic toxicity studies. The ASTM protocols contain detailed guidance regarding appropriate animal husbandry and water quality to enable proper growth and survival of the test organisms, including frogs. Consequently, the Agency concluded that the conduct of each of the laboratory studies was sufficiently compromised that it was not possible to determine whether the conditions of the study, independent of atrazine, were responsible for the observed effects, or the lack thereof. In addition, the laboratories did not use consistent protocols for preparation and examination of tissues (both visually and microscopically). They did not employ standard terminology for

describing microscopically observed abnormalities. These flaws across all the laboratories' studies resulted in uncertainties in the analysis and interpretation of the potential atrazine-related effects on amphibian development.

(I note that Dr. Hayes claims not only that his laboratory has repeated his findings many times in experiments with thousands of frogs, but that other scientists have also replicated his results. EPA, however, has never seen either the results from any independent investigator published in peer-reviewed scientific journals or the raw data from Dr. Hayes' additional experiments that confirm Dr. Hayes' conclusions.)

Finally, in regard to field studies, the Agency concluded that all these studies, either those performed under contract for Syngenta or performed by Dr. Hayes or others, had limited value. All these field studies have serious design or methodological flaws that limit their usefulness in assessing the potential effects of atrazine on frog development in the wild. Some of the problems included designation of "control" sites with concentrations of atrazine higher than the concentrations in some of the "exposure" sites and the failure to evaluate potential non-chemical stressors such as nutrient loading and habitat conditions which stress the animals and confound results.

In sum, because of the pervasive problems with all of the data, EPA concluded that, while the research raised questions about possible effects on frogs, scientifically valid conclusions could not be drawn with the level of confidence scientists routinely expect. These questions were, nonetheless, worthy of further investigation. To ensure the credibility and soundness of additional research, the Agency developed a 5-phase research proposal outlined in the White Paper.

EPA took its White Paper to the SAP to obtain an independent, objective, expert review of our conclusions. Before describing the details of that process, I want to address the widely-reported (and erroneous) statements that the conclusions of this SAP are not credible because of the conflict of interest of its chairman, Dr. Ron Kendall. One critic is quoted as saying, "Talk about conflict of interest – not only was [Dr. Kendall] on the Syngenta payroll and chairing the EPA panel, he was running the lab that did all of Syngenta's work.". This allegation is untrue in one critical respect. Dr. Kendall never served on any SAP that reviewed atrazine. Because Dr. Kendall performed research for Syngenta, Dr. Kendall recused himself from participation on any matter involving atrazine or any other pesticide registered by Syngenta during his tenure on the SAP, which ended in December 2002. Thus, while Dr. Kendall did appear as a private citizen to present his and others' research results at the June 2003 SAP meeting, Dr. Kendall was no longer the chairman or even a member of the SAP at the time. He did not serve on, much less chair, the Panel or otherwise participate in the Panel's deliberations on the effects of atrazine on amphibian species.

For the atrazine SAP, we followed standard procedures to ensure that the Panel members would be impartial and reflect a range of views and expertise. In February 24, 2003, EPA announced that it would hold a public meeting of the SAP to review the White Paper and invited

public nominations for the Panel. EPA sought additional candidates for the Panel by contacting stakeholder groups, such as environmental advocacy groups and the pesticide companies' trade association, and by reviewing the scientific literature in the relevant fields. EPA carefully screened the resulting pool of candidates to identify the leading experts in the fields of amphibian toxicology and ecology, animal (particularly frog) husbandry, developmental biology and endocrinology, and ecotoxicology and risk assessment to serve on the Panel. EPA ethics officials examined financial disclosure statements to uncover any financial conflicts of interest and interviewed each prospective member for any other reason to believe the candidate might have a preexisting bias. No one who had performed research for Syngenta, an environmental advocacy group, or other critical stakeholders (or who was employed by an organization that had performed such research), or who had made statements that might create a perception of bias, was permitted to serve on the SAP. EPA eventually selected a Panel consisting of 15 members, with experts from government and academic institutions around the world, including, among others, Dr. Carl Richards from the University of Minnesota at Duluth.

(The GAO Report mentioned earlier based its favorable conclusions about the SAP on an examination of the SAP's standard operating procedures, and on an in-depth review of the application of those procedures in the case of a particular meeting. The GAO selected the June 2003 SAP meeting addressing the effects of atrazine on amphibians for that review.)

The SAP meeting followed standard procedures designed to ensure transparency and fairness including: the creation of a public docket containing all of the materials submitted for SAP review; the solicitation of advance public comments on the review materials; and the opportunity for public comment during the meeting. The actual meeting, in June 2003, lasted three days, and included about three hours of presentations by EPA, over four hours of presentation by Dr. Hayes (which included submission of additional raw data to the Panel members), as well as presentations by other stakeholders including Syngenta-sponsored researchers. After listening to these presentations, the Panel discussed publicly their responses to the scientific issues. In summary, the SAP endorsed fully EPA's conclusions about the problems with the existing data on atrazine's effects on frogs. They wrote:

> The Panel concurred with the Agency's determinations that the laboratory studies on the effects of atrazine on anuran gonadal development are sufficient to hypothesize that atrazine interferes with normal development. . . . Deficiencies in all laboratory studies were noted as related to experimental design, data analyses, or performance standards. . . . Panel members agreed sufficient data were available to establish the hypothesis . . . but were hesitant to accept the hypothesis with the limited data available. (pp. 17 - 18)

> [T]he Panel believed strongly that all of the field studies reviewed had serious design or methodological flaws that limit their usefulness in evaluating hypotheses related to the effects of atrazine on anuran [frog] developmental responses. . . . These problems render interpretation of results problematic if not impossible. (pp. 16 - 17)

The SAP also agreed with EPA that further well-designed and conducted studies on the potential effects of atrazine on frogs were needed and endorsed the Agency's 5 phase research proposal.

Since the SAP meeting, Syngenta has initiated the required studies in Phase 1, following a GLP-compliant protocol reviewed by EPA. The Phase 1 studies should establish whether or not exposure to atrazine can cause changes in gonadal development and reproduction in frogs. To date, there are no results from this testing; a report on this research is due early in 2006. EPA expects to review these results and incorporate them into its RED for August 2006. Positive results could trigger regulatory restrictions and /or Phase 2, 3 and 4 studies to characterize the mechanism of atrazine toxicity. Phase 2 would measure the impacts of atrazine on estrogen (the female hormone) and testosterone (the male hormone), and Phases 3 and 4 would involve increasingly more sophisticated evaluation of the effects of atrazine on aromatase, an enzyme that is involved in the conversion of testosterone to estrogen. Depending on the results of Phases 2, 3, and 4, EPA may require the registrant to conduct Phase 5 studies to assess the ecological relevance of the laboratory observations to field conditions. Because there are no standardized test methods for any of these studies, EPA expects to continue to work closely with the SAP and registrant on the interpretation of the data resulting from this research and on the design of any additional studies needed.

Atrazine and Effects on the Mammalian Endocrine System

It has been claimed that research on frogs shows that atrazine causes changes in the production of aromatase, an enzyme that is involved in the conversion of testosterone to estrogen. It has also been claimed that other scientists have shown similar effects in other species. Based on the similarity of the metabolic systems across species, it has been argued, atrazine might disrupt the functioning of the human endocrine system, leading to such adverse effects as breast cancer. EPA does not agree that available frog research emphatically shows the effects of atrazine on the frog endocrine system and thus the likelihood for similar outcomes in humans.

There is no direct scientific information to assess this hypothesis. In the absence of such information, EPA has considered this theory and concluded that it is not supported by the overall weight of the evidence on the toxicity of atrazine in mammalian test species, nor is it consistent with the available human data. First, the AHS has found no association between breast cancer and exposure to atrazine. Second, the SAP has reviewed the available data on how experimental animals handle atrazine and concluded that atrazine is not likely to be carcinogenic in humans. Of course, we are fully prepared to reexamine this conclusion in light of new scientific information.

Conclusion

Clearly, there is an active debate about the safety of atrazine. After a very careful assessment, EPA's current view is that the available studies do not adequately demonstrate such

effects. A panel of independent, external experts, the SAP, supports EPA's position. At the same time, we hope it is clear the Agency is committed to fully understanding whether atrazine has the potential to harm amphibians and humans. To resolve these questions, EPA has required new research, is monitoring the progress of ongoing research, and will analyze all of these data as they become available. Finally, if data show atrazine harms wildlife or humans, EPA will aggressively pursue regulatory measures necessary to ensure atrazine will be used only if it is safe for people and the environment.

Attachment 1

List of the members of the FIFRA Scientific Advisory Panel meeting on June 17 - 19, 2003 regarding "Potential Developmental Effects of Atrazine on Amphibians".

Stephen M. Roberts, Ph.D., FIFRA SAP Session Chair and permanent SAP member
Professor and Program Director
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Center for Environmental & Human Toxicology

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Institute for Social Research
University of Michigan

Gary E. Isom, Ph.D., permanent SAP member
Professor of Toxicology
School of Pharmacy and Pharmacal Sciences
Purdue University

Fumio Matsumura, Ph.D., permanent SAP member
Professor
Institute of Toxicology and Environmental Health
University of California at Davis

Mary Anna Thrall, DVM, MS, permanent SAP member
Diplomate, ACVP
Department of Microbiology, Immunology and Pathology
Colorado State University

Joel Coats, Ph.D.
Professor and Chair
Department of Entomology
Iowa State University

Peter Delorme, Ph.D.
Senior Evaluation Officer
Environmental Assessment Division
PMRA, Health Canada

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Associate Professor and Associate Chair for Undergraduate Studies
Department of Molecular, Cellular and Developmental Biology

Associate Professor
Department of Ecology and Evolutionary Biology
The University of Michigan

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Leibniz-Institute of Freshwater Ecology and Inland Fisheries

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Carl Richards, Ph.D.
Director and Professor
MN Sea Grant College Program
University of Minnesota Duluth

David Skelly, Ph.D.
Associate Professor of Ecology
Yale School of Forestry and Environmental Studies