HAYES FROG DATA FLUNKED INDEPENDENT PEER REVIEW

“Hayes is not an impartial observer of these events…. A truly independent assessment of his interpretation and conclusions would be helpful.”

John Peterson Myers (Publisher of “Our Stolen Future” Website).

“I don’t think I would want to conduct a risk assessment with the data that’s been presented.”

Dr. Peter Delorme (during independent peer review of Hayes frog data)

Dr. Tyrone Hayes, a professor at the University of California at Berkeley, is waging a personal war against the herbicide atrazine. Dr. Hayes claims his laboratory tests and field studies demonstrate that atrazine causes gonadal deformities in frogs. He further claims the United States Environmental Protection Agency improperly allowed continued use and sale of atrazine when his data show that it should be banned.

In his standard stump speech, Dr. Hayes claims EPA improperly relied on tests and studies that contradict his data. He claims these other tests and studies were perverted by the fact that they were funded by Syngenta, the company that manufactures atrazine. Whenever he gets the chance, Dr. Hayes argues that his data are good science and the contradictory data are bad science corrupted by industry influence.

For example, Dr. Hayes recently made his claims during testimony before the Minnesota State Legislature in support of introduced bills that would ban atrazine in the State. This legislation was not enacted despite Dr. Hayes’s best efforts.

As another example, the environmental group “Our Stolen Future,” has provided Dr. Hayes with a forum on its web site to attack atrazine, Syngenta, EPA, his fellow scientists and anyone else who dares disagree with him or question his work. The centerpiece of this Internet forum is an article that Dr. Hayes wrote for the magazine BioScience. The Hayes

1 Transcript of Hayes Testimony before Minn. Senate Environment and Natural Resources Committee on 10/26/04 (“Minn. Testimony”), copy available at ______. Dr. Hayes’s testimony will heinafter be referred to as “Minn. Testimony.”


3 The BioScience article is only available on the Stolen Future web site if you pay for it. It can, however, be accessed for free at
web site provides the following caveat by its publisher:

“Hayes is not an impartial observer of these events..., as his studies have been subject to repeated attacks by EcoRisk associated scientists [Ecorisk is the group of scientists funded by Syngenta at EPA’s request to review atrazine]. A truly independent assessment of his interpretation and conclusions would be helpful.”

This reasonable request has already been granted. “A truly independent assessment” of Dr. Hayes’s work has already occurred, although Dr. Hayes never seems to mention it.

In 2003, EPA convened a Science Advisory Panel (“SAP”) to review all data regarding atrazine frog effects, including Dr. Hayes’s data. The SAP was comprised primarily of academics. None of the Panel members were on the Syngenta payroll. The Panel members were selected not only for their independence, but also for their expertise in frogs.

The SAP’s review included a three-day public meeting during which anyone could comment. Dr. Hayes’s comments consumed almost an entire day of the meeting.

During its public meeting, the SAP reviewed a hundred-page draft EPA report on atrazine’s frog effects. The draft EPA report discussed all the available data extensively, including Dr. Hayes’s data. The draft EPA report was also subject to public comment.

After extensive review, and after extensive public comment including Dr. Hayes’s own

http://www.iceh.org/pdfs/SBLF/HayesBioscience.pdf. The article will be hereinafter be referred to as “BioScience.”


The list of Panel members is available at the following URL:

Dr. Hayes’s testimony at the SAP public meeting can be viewed at the following URL, beginning at page 92: http://www.epa.gov/scipoly/sap/2003/june/061803transcript.pdf

The EPA report is available at the following URL:
lengthy presentation, the SAP—a panel of unbiased experts in the field—reached several conclusions regarding Dr. Hayes’s data and the other data on atrazine frog effects. Those expert, objective conclusions are discussed in detail below. They are summarized here as follows.

- “[T]here is not sufficient scientific evidence to indicate that atrazine consistently produces effects across the range of amphibian species examined.”
- “[T]here were deficiencies and uncertainties with respect to the methods, conduct, and results of the studies submitted. Given these deficiencies and limitations, the panel concluded that the current data would not be suitable for ecological risk assessment.”
- “The panel concluded that although they agreed that a causal relationship can be hypothesized between atrazine and effects on gonadal development, the uncertainties and deficiencies in existing studies precluded acceptance of the hypothesis....”

In other words, an unbiased panel of experts in the field concluded that Dr. Hayes’s data warranted further investigation of the atrazine frog effects issue, but that flaws and deficiencies in the all the data, including Dr. Hayes’s, precluded EPA’s use of the data for its atrazine risk assessment.

The SAP’s conclusion was perhaps most succinctly stated by Panel member Dr. Peter Delorme: “Certainly, I don’t think I would want to conduct a risk assessment with the data that’s been presented.”

If Dr. Hayes or anyone else wants to challenge the SAP’s integrity or expertise, then the Panel members’ individual contact information is provided in the following footnote.

The SAP’s conclusions about Dr. Hayes’s most important claims are provided below. Unless the context otherwise requires, each Hayes claim will be presented first, followed by the SAP’s conclusion about that claim.

**LAB TESTS**

Laboratory tests consist of raising frogs in laboratories, exposing them to atrazine in the labs, and examining them for atrazine effects.

1. Hayes’s Claim

Dr. Hayes claims his and other researchers’s lab tests demonstrate that atrazine at very

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8 SAP Report, p. 25.
9 SAP Report, p. 25.
10 SAP Report, p. 25.
11 FIFRA SAP, Open Public Meeting (June 19, 2003), Public Meeting Transcript, p. 219 (“III Public Meeting”. The transcript of the cited portion of the SAP Public Meeting is available at the following URL: http://www.epa.gov/scipoly/sap/2003/june/061903transcript.pdf The transcripts of the previous two days of the SAP public meeting are available at the following URL: http://www.epa.gov/scipoly/sap/2003/index.htm#061703
12 http://www.epa.gov/scipoly/sap/2003/june/panelmembers.htm
low and environmentally relevant doses causes gonadal deformities in frogs. E.g.,

A) BioScience, p. 1139: Dr. Hayes claims his lab tests showed that “[a]trazine at levels of 0.1 ppb or higher produced gonadal deformities [in frogs], including multiple testes, nonpigmented ovaries (or what appeared to be ovaries); and hermaphrodites....”

B) BioScience, p. 1139: “We also showed that males were in fact chemically castrated when exposed to atrazine..., and we have subsequently shown that this effect occurs at doses as low as 0.01 ppb in adult males.”

C) BioScience, p. 1140: “Like the studies performed by my laboratory, the [industry-financed] study by Carr and colleagues (2003) showed that atrazine exposure resulted in gonadal deformities.”

D) Minn. Testimony, p. 8: “In our initial laboratory model, we showed in the African clawed frog that atrazine castrated males.”

E) Minn. Testimony, pp. 10-11: “What I’m going to show you now is the effect of exposing animals to atrazine. Starting at 0.1 parts per billion, we produced poorly developed testes...as well as what I’m calling testicular ovogenesis meaning eggs have grown in the testes of these animals.”

F) Minn. Testimony, p. 18: “We have very clear control studies in the laboratory that show we can induce [frog] hermaphrodites. We have a clear correlation between hermaphroditism and atrazine contamination.”

2. SAP Peer Review of Claim

After reviewing all the relevant lab test data, including Dr. Hayes’s, the SAP concluded that there were flaws and deficiencies in all the lab tests, and that the flaws and deficiencies precluded acceptance of Dr. Hayes’s claim that the tests demonstrated or showed atrazine effects on frog gonads. Given the current data, including Dr. Hayes’s data, the Panel concluded that atrazine effects on frogs were only an unproven “hypothesis.” E.g.,

A) SAP Report p. 18: After carefully reviewing all the relevant lab tests, including Dr. Hayes’s tests, the SAP stated:

“Deficiencies in all laboratory studies were noted as related to experimental design, data analyses, or performance standards.

“Significant data gaps exist in our understanding of the effects of atrazine on anuran [frog] development. These gaps include a lack of understanding of the mechanism by which atrazine might elicit developmental toxicity, the nature of the concentration-response relationship, definition of susceptible windows of exposure, variable
terminology used to describe effects, and definition of a threshold concentration. Panel members agreed that sufficient data were available to establish the hypothesis that atrazine interferes with normal gonadal development but were hesitant to accept the hypothesis with the limited available data. It was agreed that more data were necessary to properly test the hypothesis. These data should be generated under standardized conditions and must be subject to independent verification.

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“A major deficiency that exists among laboratory studies of the effects of atrazine on anuran gonadal development has been the difficulty in defining the concentration-response relationship, and accordingly, a threshold concentration.”

B) SAP Report p. 25:

“The first conclusion put forth [by EPA] was: ‘there is not sufficient scientific evidence to indicate that atrazine consistently produces effects across the range of amphibian species examined.’ The Panel agreed with this conclusion....The response of the species, both in terms of the endpoints considered and the magnitude of response, was inconsistent across the species studied and among studies which used the same species. Comparison among the studies was difficult because of the problems identified with respect to the design and conduct of both the laboratory and field studies, which confound their interpretation.”

C) SAP Report p.25 :

“The second conclusion put forth [by EPA] was that ‘the current body of knowledge has deficiencies and uncertainties that limits its usefulness in assessing potential developmental atrazine effects!’ The Panel agreed with the conclusions in the Agency’s White Paper that there were deficiencies and uncertainties with respect to the methods, conduct, and results of the studies submitted....Among the major factors identified were difficulties with the husbandry in laboratory studies, presence of atrazine in control exposures and reference sites and a lack of consideration of and/or information on the presence or potential impact of other stressors in observational field studies. Given these deficiencies and limitations, the Panel concluded that the current data would not be suitable for ecological risk assessment. Further, it was recognized by the Panel that in order to conduct a scientifically sound ecological risk assessment, the Agency needs to have results from studies where other factors can be ruled out as a cause in either the presence or the absence of effects.”

D) SAP report pp 25-26:

“The third conclusion put forth [by EPA] was that the uncertainties and deficiencies limited ‘the extent of (the identification of) any associated cause-effect and concentration-response relationships.’ The Panel concluded that although they agreed
that a causal relationship can be hypothesized between atrazine and effects on gonadal development, the uncertainties and deficiencies in existing studies precluded acceptance of the hypothesis..... Further, the exact nature of the response in gonadal development in amphibians (shape of the concentration/response function, presence of a threshold) cannot be characterized at this point for the species tested....Finally, the Panel noted that knowledge of the concentration/response function is a necessary element to conduct an ecological risk assessment.”

E) SAP report p. 26:

“The final conclusion put forth [by EPA] was: “the Agency has determined that there are not sufficient data to reject the hypothesis that atrazine can cause adverse developmental effects in amphibians.” The Panel agreed that the available data suggest that atrazine can affect gonadal development in amphibians. However, the available data do not allow a proper characterization of the nature and magnitude of the response at either the organism or population level, nor do they offer sufficient support for the identification of a plausible mechanism.”

F) SAP Report p. 26:

“The Panel agreed with the [EPA] conclusion that additional information is required to evaluate potential causal relationships between atrazine exposure and gonadal development. Several points were made in regard to this conclusion. There is a need to confirm the causal relationship that is suggested by the existing data, and some similarity of data, or patterns or trends, from different labs needs to be presented to show repeatability of the effects. One of the tenets of the scientific method is the repeatability of experiments. Further, as previously noted, it is necessary to characterize the nature of the dose-response (or more correctly, concentration-response) function. Finally, there is a need to identify a plausible mechanism, supported by data. The characterization of a mechanism can, in part, aid in the extrapolation of results from surrogate test species to species of concern in the environment.”

G) III Public hearing, pp 217-19:

“[T]he inconsistency of the response across a species studied was difficult to assess because of the problems identified with respect to the design and conduct off both the laboratory and the field study.” [SAP member Dr. Peter Delorme].

**FIELD TESTS**

Field tests, as opposed to lab tests, consist of gathering frogs in the wild and then examining them for effects caused by exposure to atrazine in the wild.
1. Hayes Claim

Dr. Hayes claims he found frogs exposed to atrazine in the wild that show the same
gonadal deformities that he claims too have found in lab-exposed frogs. E.g.,

A) Minn. Testimony, p. 16:

“Leopard frogs live over this range. Here are the sites we looked at. The red now shows
you all the sites where we find hermaphrodites, and it’s associated with atrazine in the
water, in the groundwater and surface water 100 percent of the time.”

B) Minn. Testimony, p. 16:

Describing a frog he found in Wyoming, Dr. Hayes says, “It’s chemically castrated, it’s
infertile, no sperm and it’s feminized. It’s got eggs that in the spring it will try to yolk
up.”

C) Minn. Testimony, p. 17:

[W]here you find atrazine, you find [frog] hermaphrodites....[W]hen you find atrazine,
you find hermaphrodites. And if you clean up the atrazine, the animals return to normal.
It shows us that this site is not just a site where there’s natural hermaphroditism. Those
animals are only hermaphrodites when there’s atrazine contamination at that river.”

2. SAP Peer Review of Claim

After reviewing all the relevant field studies, including Dr. Hayes’s, the SAP concluded
there were flaws and deficiencies in all the field studies, and that the flaws and deficiencies
precluded acceptance of Dr. Hayes’s claim that the studies demonstrated or showed atrazine
effects on frog gonads. Given the current data, including the data from Dr. Hayes’s field studies,
the Panel concluded that atrazine effects on frogs were only an untested “hypothesis.” E.g.,

A) SAP report, pp. 16-17:

“The Panel concluded that the absence of an established causal relationship derived from
laboratory studies was not critical in limiting the interpretation of the field studies.
Ecological field studies are routinely, and successfully, conducted in the absence of such
information. However, the 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 exposure on anuran developmental responses.
Common, important problems in the field studies considered included inappropriate site
selection practices (e.g., designation of control sites with concentrations of atrazine that
exceeded some exposure sites) and failure to identify a sampling frame and to choose
sampling sites randomly from within it, as well as insufficient statistical power associated with too few sampling sites to evaluate study hypotheses. These problems render interpretation of results problematic, if not impossible.”

“It also was noted that the field studies focused on measurement of endpoints identified in laboratory studies. None of the field studies measured responses for which field studies are most revealing. Specifically, whereas abundance and age structure were measured occasionally, highly relevant endpoints related to reproduction, recruitment and population viability were entirely absent. It should also be noted that, aside from one mesocosm experiment, all of the field studies were observational. While observational field studies are necessary and potentially yield strong inference, carefully designed field experiments offer opportunities to manipulate the natural environment, thereby controlling for some potentially confounding factors and allowing direct interpretation of responses. Such an opportunity was unexploited in the pool of field studies considered by the Panel.”

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“The Panel concluded that the field studies conducted to date do not, however, provide sufficient information to resolve the potential role of additional co-occurring stressors....”

B) SAP Report, p. 25:

“The response of the species, both in terms of the endpoints considered and the magnitude of the response, was inconsistent across the species studied and among studies which used the same species. Comparison among the studies was difficult because of the problems identified with respect to the design and conduct of both the laboratory and field studies, which confound their interpretation.”

C) III Public Hearing, pp 217-19:

“[T]he inconsistency of the response across a species studied was difficult to assess because of the problems identified with respect to the design and conduct of both the laboratory and the field study.” [SAP Member Dr. Peter Delorme].

FLOW THROUGH Vs. STATIC:
A SPECIFIC LAB TEST DESIGN PROBLEM

Dr. Hayes’s lab tests, and all the other lab tests, were conducted with static water conditions for the test frogs. There wasn’t a steady flow of water through the test frog tanks. The SAP questioned this practice. E.g., III Public Meeting, pp. 303-28.
FAILURE TO TEST WATER FLOWING INTO FROG PONDS:  
A SPECIFIC LAB TEST DESIGN PROBLEM

Dr. Hayes’s field studies, and all the other field studies, failed to test for critical parameters the water flowing into the water bodies from which frogs were taken for analysis. The SAP questioned this practice. E.g., III Public Meeting, p. 134.

HAYES’S USE OF ONLY THREE BREEDING PAIRS:  
A SPECIFIC LAB TEST DESIGN PROBLEM

One SAP member criticized Dr. Hayes’s lab tests because all the frogs he tested originated from only three breeding pairs. E.g.,

A) SAP Report, p. 29;

B) III SAP Public Meeting, pp. 329-30 [Dr. Gibbs]:

“I still have lingering concerns that far too individuals use the found [SIC], the experimental larval populations in some of these laboratory studies. It is not my area of expertise, but as a population geneticist, it really concerns me when three pairs are used. One onymous [SIC] individual with three pairs will potentially skew an entire experiment. I think boosting numbers up into the 10s of pairs, I think it seems like a good idea to me.”

AROMATASE INDUCTION AS MECHANISM OF ACTION

1) Hayes Claim

Dr. Hayes claims that atrazine causes gonadal effects in frogs by inducing their production of the hormone aromatase. E.g., Minn. Testimony, p. 7; BioScience, pp. 1139-40.

2) SAP Peer Review of Claim

The SAP, after reviewing all the available data, including Dr. Hayes’s, concluded that the data do not show that atrazine induces aromatase production or that aromatase induction causes gonadal effects in frogs. This SAP conclusion was based in part on flaws and deficiencies in the data, including Dr. Hayes’s data. E.g.,

1) SAP report, p. 20:

“The Panel agreed with the Agency’s [EPA’s] conclusion that, to date, aromatase induction by atrazine has not been demonstrated in anurans by controlled laboratory studies. The experimental designs used by several investigators in order to demonstrate effects on aromatase induction using long term exposures are
inappropriate to demonstrate any influence of atrazine, if there might be one.”

2) III SAP Public Meeting, pp. 176, 178- 179, 181 (SAP members state that aromatase induction has not been demonstrated because the experiments were poorly designed)

**NEED FOR VALIDATED, STANDARDIZED TEST PROTOCOLS**

The SAP emphasized the need for new, standardized, validated test protocols that must be followed in any future test/studies of the effects of atrazine on frogs. The SAP provided detailed recommendations for these new test/studies. Neither Dr. Hayes’s test/studies, nor anyone else’s, have so far been performed in accordance with these recommended new procedures. E.g.,

A) SAP Report, pp. 28-29:

“The Panel was in consensus that a clear set of definitions concerning the terminology for classifying gonadal deformities should be developed by the Agency. This is essential for quantifying results of past and future studies. Regarding the major sources of uncertainty associated with the potential effects of atrazine on anuran sexual differentiation, the Panel agreed with the Agency that the lack of standardization of husbandry protocols for laboratory *Xenopus laevis* and *Rana pipiens* likely played a significant role. The Panel is aware that the Agency has expertise in these areas. The Panel concurred that ASTM guidelines for water quality should be followed. For example, pH, conductivity, ammonia (total, ionized and unionized forms), nitrate, nitrite, dissolved oxygen, chloride or chloramine levels, copper and iron levels should be standardized among experiments. Alterations in any of these parameters may alter experimental results, particularly those involving growth rates and development. With FETAX, Holtfreter’s solutions with adequate calcium are adequate for raising tadpoles.”

“Animals should be loaded in flow-through tanks at a density according to ASTM guidelines. Flow through tanks are preferable, but data collected from static renewal tanks would be acceptable provided animals are loaded according to ASTM guidelines and water quality is assessed on a daily basis (and maintained within the ASTM guidelines). *Xenopus laevis* are carnivores. Therefore, diet should contain at least 14% protein. Diets formulated for herbivores or for omnivorous fish or turtles are not suitable. Diets formulated especially for *Xenopus* are commercially available for both tadpoles and adults. The quantity of feed (g/animal) should be based on the manufacturer’s recommendation and adjusted as the animal grows. “

“The following reference is recommended as a guide for housing and husbandry of anurans: Amphibian Medicine and Captive Husbandry. (Eds.): KM Wright and BR Whitaker, Krieger Publishing Co., Malabar, FL.”

“One Panel member felt that a larger number of male/female pairs should be used to develop tadpole treatment groups. The current use of three pairs is minimal and may contribute to variation in results among experiments reported to date”.

“One Panel member believed that a stock colony of *Xenopus* animals should be
developed that researchers could draw upon. This would minimize potential variation among populations studied in different laboratories. This stock colony should include phenotypic females with a ZZ genotype so that sex ratios can be accurately determined.”

**CONCLUSION**

If Dr. Hayes continues to attack atrazine--and if he wishes to be objective and rational---then he should state that a panel of independent, expert peer reviewers advised EPA not to rely on Dr. Hayes’s data during the atrazine re-registration proceeding because those data were too flawed and incomplete to use in a regulatory risk assessment.