FACA COMMITTEE FINDS FLAWS IN HAYES FROG TESTS AND DATA

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The Center for Regulatory Effectiveness
11 Dupont Circle, NW
Washington, DC 20036
202.265.2383
www.theCRE.com

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>
> – 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 (Senior Evaluator, Pest Management Regulatory Agency, Health Canada, during FACA review of Hayes' frog tests and data)

Dr. Tyrone Hayes, a professor at the University of California at Berkeley, is waging a personal and very public 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 ("EPA") improperly allowed the continued use and sale of atrazine when his data show that it should be banned.

In his standard stump speech, Dr. Hayes blames EPA's decision on the Agency's reliance 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 the manufacturers of atrazine, in particular a company named Syngenta. 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 testified before the Minnesota State Legislature in support of introduced bills that would ban atrazine in the State.[1] This legislation was not enacted despite Dr. Hayes' 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, atrazine's manufacturers, EPA, his fellow scientists and anyone else who dares to disagree with him or question his work.[2] The centerpiece of this Internet forum is an article that Dr. Hayes wrote for the magazine *BioScience.*[3]

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[1] Transcript of Hayes Testimony before Minn. Senate Environment and Natural Resources Committee on 10/26/04 ("Minn. Testimony").

[2] http://www.ourstolenfuture.org/NewScience/wildlife/frogs/2004/2004-1201hayes.htm

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

The 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.***[4]

This reasonable request has already been granted. "A truly independent assessment " of Dr. Hayes' tests and data has already occurred.

In 2003, EPA convened a Science Advisory Panel ("SAP") to review all data regarding atrazine's frog effects, including Dr. Hayes' data. The SAP is a Federal Advisory Committee Act ("FACA") committee of scientists established under the Federal Insecticide, Fungicide and Rodenticide Act ("FIFRA").[5] The SAP found flaws in all the tests and data on atrazine frog effects, including those of Dr. Hayes and those financed by Syngenta (a manufacturer of atrazine).

Contrary to Dr. Hayes' claims and publicity campaign, EPA did not rely on Syngenta-financed tests when the Agency decided not to use Dr. Hayes' tests and data to regulate atrazine. Instead, EPA relied on the SAP's conclusion that **all** the available tests and data were flawed, including Dr. Hayes'. It is this FACA committee's conclusion that Dr. Hayes challenges and refuses to accept.

Background On The SAP Atrazine Review

The Government Accounting Office in a report on FACA committees praised the atrazine SAP as a model of independence and balance.[6] The atrazine SAP was comprised primarily of academics. None of the SAP members had done any work for atrazine's manufacturer. The Panel members were selected not only for their independence, but also for their expertise in the area of frogs.[7]

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[4] http://www.ourstolenfuture.org/NewScience/wildlife/frogs/2004/2004-1201hayes.htm. (statement by John Peterson Myers, Publisher of "Our Stolen Future" website).

[5] The following URL provides information about the FACA committees EPA convenes under FIFRA: http://www.epa.gov/scipoly/sap/about.htm.

[6] *Federal Advisory Committees: Additional Guidance Could Help Agencies Better Ensure Independence and Balance*, at page 73 *et seq*. (GAO 04-328 April 2004), available online at http://www.gao.gov/new.items/d04328.pdf.

[7] The Panel list is available online at the following URL: http://www.epa.gov/scipoly/sap/2003/june/panelmembers.htm

The SAP's review included a three-day public meeting during which anyone could comment. Dr. Hayes' comments consumed almost an entire day of the meeting.[8]

During the public meeting, the SAP reviewed a hundred-page draft EPA report on potential effects of atrazine on frogs. The draft EPA report discussed all the available data extensively. These data included the results of extensive tests paid for by Syngenta, Dr. Hayes' data, and other test data unrelated to either Syngenta or Dr. Hayes. The draft EPA report was also subject to public comment.[9]

After extensive review, and after extensive public comment including lengthy presentations by Dr. Hayes and Syngenta, the SAP – a FACA committee of unbiased experts in this field of research – agreed with and approved all of EPA's conclusions regarding Dr. Hayes' tests and data and all the other tests and data regarding atrazine's frog effects. EPA's conclusions included the following.

- **"[T]here is not sufficient scientific evidence to indicate that atrazine consistently produces effects across the range of amphibian species examined"**[10]
- **"[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."**[11]
- "**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...."**[12]

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[8] Dr. Hayes' testimony at the SAP public meeting can be viewed online at http://www.epa.gov/scipoly/sap/2003/june/061803transcript.pdf (beginning at page 92). This online transcript of the public hearing will hereinafter be cited as "Hearing Trans."

[9] The EPA report is available online at http://www.epa.gov /scipoly/sap/2003/june/finaljune2002telconfreport.pdf.

[10] Meeting Minutes of the FIFRA Scientific Advisory Panel Meeting Held June 17-20, 2003, p. 25 (emphasis added), available online at http://www.epa.gov/scipoly/sap/2003/june/junemeetingreport.pdf. The report will hereinafter be cited as "*SAP Report*."

[11] *SAP Report*, p. 25 (emphasis added).

[12] *SAP Report*, p. 25 (emphasis added).

In other words, an unbiased FACA panel of experts in this field of research concluded that Dr. Hayes' frog tests and data, as well as other studies submitted, warranted further investigation of the atrazine frog effects issue. The SAP also concluded that flaws and deficiencies in the all the data, including Dr. Hayes', 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.***[13]

Syngenta has accepted the SAP's conclusion that further investigation is warranted. Syngenta is now trying to develop and perform tests that conform to the SAP's comments.
Protocols have been reviewed by EPA.

By contrast, Dr. Hayes refuses to accept the SAP's criticism of his tests and data. Rather than learn from the SAP and improve his research, Dr. Hayes is conducting a public relations campaign to impugn EPA and EPA's independent, expert FACA committee: the SAP.

In order to provide the public with the facts of this controversy, the Center for Regulatory Effectiveness ("CRE") is presenting the SAP's conclusions about Dr. Hayes' tests below.

First, CRE will present the SAP's reasons for agreeing with EPA's conclusions that it could not use Dr. Hayes' tests and data.

Second, CRE will present in detail the SAP's review of Dr. Hayes' laboratory tests and data.

Third, CRE will present in detail the SAP's review of Dr. Hayes' field tests and data.

Fourth, CRE will present in detail the SAP's review of Dr. Hayes' claim that atrazine causes adverse effects in frogs by inducing aromatase.

Fifth, in conclusion, CRE will present in detail the SAP's recommendation that new, standardized test procedures be developed and used after they have been proven accurate and reliable. Dr. Hayes still refuses to accept the possibility that there may be flaws in his tests even after the SAP identified them for him.

In the following discussion, Dr. Hayes' claims about his tests and data will generally be presented first, followed by the SAP's conclusion about the claims. In some cases, this format will be varied to address Dr. Hayes' specific test procedure first, followed by the SAP's critical review of that procedure.

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[13] *III Hearing Trans*., p. 219 (emphasis added).

The SAP Agreed With All Of EPA's Conclusions About Hayes' Tests and Data

EPA's draft report to the SAP contained the Agency's conclusions regarding Dr. Hayes' tests and data, and about all other available tests and data on atrazine's effects on frogs**,** including Syngenta's**.** The SAP agreed with all of EPA's conclusions.

EPA's first conclusion was that,

> ***'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.***[14]

EPA's second conclusion 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*.**
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> ***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.***[15]

EPA's third conclusion was,

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[14] *SAP Report,* p. 25 (emphasis added).

[15] *SAP Report,* p.25 (emphasis added).

> ***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.***"[16]

EPA's fourth conclusion was 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.***[17]

Finally, the SAP agreed with EPA,

> ***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.***[18]

SAP member Dr. Peter Delorme further commented on the test flaws during the SAP public hearing:

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[16] *SAP Report,* pp 25-26 (emphasis added).

[17] *SAP Report,* pp 25-26 (emphasis added).

[18] *SAP Report,* p 26 (emphasis added).

> ***[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.***[19]

The "problems" identified by the SAP prevented use of any of the available tests and data, including Dr. Hayes' tests and data.

The SAP Found Flaws In Hayes' Lab Tests and Data

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

1. Hayes' Claim

Dr. Hayes claims that his and other researchers' lab tests demonstrate that atrazine at very low and environmentally relevant doses causes gonadal deformities in frogs.[20]

2. SAP Review of Claim

After reviewing all the relevant lab tests, including Dr. Hayes', 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' claim that the tests demonstrated atrazine effects on frog gonads. Given the current data, including the data from Dr. Hayes' tests, the Panel concluded that atrazine effects on frog gonads were only an untested "hypothesis."

For example, after carefully reviewing all the relevant lab tests, including Dr. Hayes' tests, the SAP stated, "**Deficiencies in all laboratory studies were noted as related to experimental design, data analyses, or performance standards**."[21]

For example,

> ***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.***[22]

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[19] *III Hearing Trans.,* pp 217-19 (emphasis added).

[20] *E.g.,* BioScience, pp. 1139-40; Minn. Testimony, pp. 8, 10-11, 18.

[21] *SAP Report,* p. 18 (emphasis added).

[22] *SAP Report,* p. 18 (emphasis added).

Two other SAP examples of flaws in frog raising – static water and use of only three breeding pairs – are discussed below.

Use of Static Instead of Flow Through Water

1. Hayes Procedures

Dr. Hayes' lab tests, and all the other lab tests, were conducted with static water conditions for the test frogs. In other words, there wasn't a steady flow of water through the test frog containers.

2. SAP Review of Hayes Procedures

The SAP questioned Dr. Hayes' static water procedure and recommended using flow through instead of static in order to optimize environmental rearing conditions.[23]

Use of Only Three Breeding Pairs

1. Hayes Frog Breeding Practices

As of the date of the SAP meeting, all of the frogs in Dr. Hayes' labs came from only three breeding pairs of frogs.

2. SAP Review of Hayes Frog Breeding Practices

The SAP criticized this limited number of breeding pairs because it could create in-breeding problems and did not provide sufficient genetic diversity. For example, one SAP member commented:

> ***It is not my area of expertise, but as a population geneticist, it really concerns me when three pairs are used. One anonymous 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.***[24]

The SAP Found Flaws In Hayes' Field Tests and Data

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.

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[23] *E.g., III Hearing Trans.*, pp. 303-28.

[24] *III Hearing Trans.*, pp. 329-30 (Dr. Gibbs)(emphasis added); *accord SAP Report*, p. 29 (more breeding pairs should be used).

1. Hayes Claim

Dr. Hayes claims that he found frogs exposed to atrazine in the wild that show the same gonadal deformities that he claims to have found in lab-exposed frogs.[25]

2. SAP Review of Claim

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

Relevant passages from the SAP Report are set forth below:

> ***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.***
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> ***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***

[25] *E.g.*, Minn. Testimony, pp. 16-17.

> ***responses. Such an opportunity was unexploited in the pool of field studies considered by the Panel.***[26]
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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....*** [27]
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> ***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.***[28]
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> ***
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> ***[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.***[29]

Failure to Test Water In Frog Ponds: A Specific Hayes Field Test Design Problem

1. Hayes Procedures

Dr. Hayes' field studies, and all the other field studies, failed to test the water flowing into the ponds for critical parameters.[30]

2. **SAP Review of Hayes Procedure**

The SAP questioned Dr. Hayes failure to test for critical parameters. The SAP recommended that this critical parameter testing be performed.[31]

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[26] *SAP Report*, pp. 16-17 (emphasis added).

[27] *SAP Report*, pp. 16-17 (emphasis added).

[28] *SAP Report*, p. 25 (emphasis added)

[29] *III Hearing Trans.,* pp 217-19 (Dr. Delorme)(emphasis added).

[30] *E.g., III Hearing Trans*., p. 134.

[31] *E.g., III Hearing Trans*., p. 134.

The SAP Found Flaws In Hayes' Claim That Atrazine Induces Aromatase

1. Hayes Claim

Dr. Hayes claims that atrazine causes gonadal effects in frogs by inducing their production of the hormone aromatase.[32]

2. SAP Review of Claim

The SAP, after reviewing all the available data, including Dr. Hayes', concluded that they do not show: (i) that atrazine induces aromatase production; or that (ii) aromatase induction causes gonadal effects in frogs. The SAP's conclusion was based in part on flaws and deficiencies in all the tests and data, including Dr. Hayes' tests and data:

> ***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.***[33]

CONCLUSION

A FACA Committee of Independent Experts Emphasized the Need for New Validated, Standardized Test Protocols

There are no tests for amphibian reproductive deformities that have been generally accepted by the scientific community as accurate and reliable. Dr. Hayes runs tests of his own design, and other scientists run differently designed tests. As demonstrated above, a FACA committee of unbiased, objective scientific experts in this field of research found flaws in all the tests, including but not limited to Dr. Hayes' tests.

Consequently, the SAP emphasized the need to develop new, standardized, validated test protocols that should be followed in any future test/studies of the effects of atrazine on frogs. These new tests must be

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[32] *E.g.,* Minn. Testimony, p. 7; BioScience, pp. 1139-40.

[33] *SAP Report,* p. 20 (emphasis added); *accord III Hearing Trans*., pp. 176, 178- 179, 181 (aromatase induction is not demonstrated because experiments were poorly designed).

shown accurate and reliable by the process of several different labs running the same tests and getting the same results. The SAP recommended that EPA set forth the ground rules for developing these new tests and that EPA oversee their development. The SAP also recommended details of the new tests.

Relevant passages from the SAP Report are set forth below:

> ***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.***[34]
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> ***
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> ***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, chlorine 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.***
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> ***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).***
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> ***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.***

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[34] *SAP Report*, p. 18 (emphasis added).

> ***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.***
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> ***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.*** [35]

One of the manufacturers, Syngenta, is implementing the FACA Committee's recommendations with protocols approved by EPA's. This complicated, expensive, time-consuming process should result in tests that reliably determine what if any effects atrazine has on frogs.

This is how science and regulation are supposed to work. Dr. Hayes' real complaint is that a FACA committee of independent scientists criticized his tests and data, and EPA incorporated the recommendations and advice from these scientific experts into the agency's regulatory process.

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[35] *SAP Report*, pp. 28-29 (emphasis added)