BEFORE THE UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY
INFORMATION QUALITY GUIDELINES STAFF

Re: Registration Eligibility Science Chapter for Atrazine: Environmental Fate and Effects Chapter (April 22, 2002) at pages 11, 90-94	)	Docket No. OPP - 34237A

REQUEST FOR CORRECTION OF INFORMATION CONTAINED IN THE ATRAZINE ENVIRONMENTAL RISK ASSESSMENT

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REQUEST FOR CORRECTION OF INFORMATION CONTAINED IN THE ATRAZINE ENVIRONMENTAL RISK ASSESSMENT

Filed by: THE CENTER FOR REGULATORY EFFECTIVENESS
AND
THE TRIAZINE NETWORK

I. ISSUE:

EPA's statements in the atrazine *Environmental Risk Assessment* regarding atrazine's endocrine effects violate government-wide data quality standards. These government-wide standards require proper test validation before the tests are considered reliable and reproducible. There are no validated endocrine-effects tests for atrazine.

II. OVERVIEW

The Center for Regulatory Effectiveness ("CRE") and the Triazine Network file this Request for Correction of EPA disseminations of information relating to the endocrine effects of the herbicide atrazine. We file this Request for Correction pursuant to the Data Quality Act amendments to the Paperwork Reduction Act[1], ("Data Quality Act"), as implemented though the Office of Management and Budget's government-wide Data Quality Act guidelines[2], ("OMB Guidelines") and EPA's Data Quality Act Guidelines[3] ("EPA Guidelines").

We request the following correction:

- EPA's final *Registration Eligibility Science Chapter for Atrazine: Environmental Fate and Effects Chapter (April 22, 2002*) *("Environmental Risk Assessment")* at pages 11, 90-94, states that atrazine causes endocrine effects in various organisms including frogs, and that it does not cause endocrine effects in other organisms[4]. These pages of the *Environmental Risk Assessment* should be corrected to state that there is no reliable evidence that atrazine causes endocrine effects in amphibians, fish, mammals or any other kind of animal because there are no validated test methods for such effects.

The Data Quality Act's Objectivity Standard requires EPA to ensure that information it disseminates is

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[1] 44 U.S.C. § 3516 statutory and historical notes

[2] 67 FR 8452 (Feb. 22, 2002)

[3] http://www.epa.gov/oei/qualityguidelines/index.html

[4] Attachment A, also available at www.epa.gov/pesticides/reregistration/atrazine

"accurate, reliable, and unbiased."[5] EPA and most other federal agencies have established a government-wide data quality standard that requires proper validation of tests before the test results can be considered reliable:

> Before a new or revised test method is used to generate information to support regulatory decisions, **it must be...validated to determine its reliability** and relevance for its proposed use.... [6] (emphasis added).

EPA's statements in the *Environmental Risk Assessment* regarding atrazine's endocrine effects violate the Data Quality Act's Objectivity Standard because there are no validated test methods for determining whether atrazine causes endocrine effects. Consequently, there are no reliable tests for these effects.

Moreover, for Influential Scientific Information, such as the *Environmental Risk Assessment*, EPA's Data Quality Guidelines require that EPA "ensure reproducibility for disseminated original and supporting data according to commonly accepted scientific, financial, or statistical methods."[7] EPA cannot ensure reproducibility of original and supporting data from atrazine endocrine-effects tests until and unless that data is generated by reliable tests, and validation is necessary to ensure reliable tests.[8]

EPA's *Environmental Risk Assessment* statements regarding atrazine's endocrine effects also violate the Data Quality Act's Utility Standard. This Standard requires that information disseminated by EPA be useful to its intended users, including the public.[9] Information from new or revised tests is not useful when it is generated from unvalidated, unreliable, unreproducible tests.

These and other points are discussed in more detail below.

III. FACTUAL BACKGROUND

Atrazine is an herbicide. The *Environmental Risk Assessment* was developed as part of EPA's review of atrazine under the Food Quality Protection Act ("FQPA") and the Federal Insecticide, Fungicide, and Rodenticide Act. The *Environmental Risk Assessment* will ultimately form part of the basis of an Interim Registration Decision ("IRED"). The IRED will determine whether atrazine can continue to be used as a herbicide and under what conditions. Under a consent decree between EPA and the Natural

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[5] 67 FR 8453, 8459 (OMB Guidelines); EPA Guidelines, p. 15.

[6] *Evaluation of the Validation Status of Toxicological Methods: General Guidelines for Submissions to ICCVAM*, Prepared by Interagency Coordinating Committee on the Validation of Alternative Methods , *et. al.*, p. v., October 1999. ("*Validation Guidelines"*) Attachment B.

[7] EPA Guidelines, p. 47.

[8] Attachment B, p. v (*Validation Guidelines)*.

[9] 67 FR 8459 (OMB Guidelines); EPA Guidelines, p. 15.

Resources Defense Council ("NRDC"), an interim IRED will be issued in January 2003. A final IRED is required by October 31, 2003. This final IRED will include review of materials on amphibian endocrine effects submitted to EPA by February 28, 2003.[10]

EPA's *Environmental Risk Assessment*, at pages 90-95, includes a section entitled "Reported Sub-Lethal Effects," which includes a subsection entitled "Endocrine Effects." This sub-section of the risk assessment first describes, without criticism, atrazine tests performed by Dr. Tyrone Hayes on frogs. According to these tests, atrazine at very low concentrations caused "gonadal abnormalities including multiple testes and/or ovarian tissues within testes (hemaphroditism)...."[11] To account for these endocrine effects, Dr. Hayes,

> ...hypothesized that atrazine induces aromatase and promotes the conversion of testosterone to estrogen. This disruption in steroidgenesis via induction of aromatase is hypothesized as a likely explanation for the 10-fold decrease in plasma testosterone, demasculization of the male larynx and the production of hermaphrodites.[12]

After discussing the Hayes frog tests, EPA concluded that:

> Atrazine effects on tadpoles are a concern because atrazine use coincides with spring rains and the breeding season for amphibians. While these gonadal abnormalities and laryngeal alterations raise concerns about adverse effects on amphibian reproduction, there is no conclusive evidence that these changes have an adverse effect on amphibian reproduction. Additional testing with atrazine-treated tadpoles and adult frogs should be conducted to determine what, if any, effects occur on reproduction.[13]

Thus, EPA's *Environmental Risk Assessment* accepts the endocrine effects allegedly shown by the Hayes Frog Tests as accurate and reliable. According to EPA, the only remaining question is whether those endocrine effects affect frogs' ability to reproduce.

The Endocrine-Effects subsection of the *Environmental Risk Assessment* also discusses tests on the effects of atrazine on estradiol, 11-ketotestosterone, testosterone, and vitellogenin in largemouth bass. EPA's *Environmental Risk Assessment* concluded:

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[10] Attachment C, p. 2.

[11] Attachment A, p. 90.

[12] Attachment A, p. 90.

[13] Attachment A, pp. 91-92.

> Although high variability confounds this study's ability to resolve the effects of atrazine on plasma steroids and vitellogenesis, the study has demonstrated that technical grade atrazine affects plasma 11-ketotestosterone in males and that the formulated product affects plasma estradiol in females. The non-guideline study is classified as supplemental and provides useful information on the potential effects of atrazine on endocrine-mediated pathways.[14]

This subsection of the *Environmental Risk Assessment* also states that atrazine causes endocrine effects in mammals:

> Based on mammalian chronic studies, the Human Health Effects Division (HED) has concluded that there is evidence that atrazine is associated with endocrine disruption. Direct measurements of norepineprine, dopamine, and GnRH, and of serum hormones such as steroid certain steroid hormones and lutenizing hormone, as well as changes in estrous cycling and histomorphic changes in hormone responsive tissues, indicate neuroendocrine disruption.[15]

Finally, EPA stated in the *Environmental Risk Assessment* that atrazine does not cause endocrine effects in daphnia, turtles or alligators.[16]

EPA reached these conclusions and disseminated this information about atrazine's endocrine effects despite the following facts:

- There are no validated tests for detecting or measuring atrazine endocrine effects in frogs.
- There are no validated tests for detecting or measuring aromatase induction.
- There are no validated test methods for detecting or measuring atrazine endocrine effects in largemouth bass.
- There are no validated test methods for detecting or measuring atrazine endocrine effects in mammals.
- There are no validated test methods for detecting or measuring atrazine endocrine effects in daphnia, turtles, or alligators.

EPA itself acknowledged this lack of validated tests in its response to comments on the *Environmental Risk Assessment:*

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[14] Attachment A, p. 93.

[15] Attachment A, p. 93.

[16] Attachment A, p. 93.

> The Endocrine Disruptor Screening program has proposed a number of test protocols for identifying endocrine effects in wildlife species. Some of these protocols are currently in round-robin testing. As of this date, none of them have been approved for regulatory testing.[17]

IV. EPA'S ENDOCRINE EFFECTS STATEMENTS VIOLATE A GOVERNMENT-WIDE DATA QUALITY STANDARD THAT REQUIRES PROPER TEST VALIDATION BEFORE THE TESTS ARE CONSIDERED RELIABLE AND REPRODUCIBLE

EPA is a member of ICCVAM. The ICCVAMs website states:

> The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) was established in 1997 by the Director of the National Institute of Environmental Health Sciences (NIEHS) to implement NIEHS directives in Public Law (P.L.) 103-43 [the 1993 NIH Revitalization Act]. This law directed NIEHS to develop and validate new test methods, and to establish criteria and processes for the validation and regulatory acceptance of toxicological testing methods. P. L. 106-545, the ICCVAM Authorization Act of 2000, established ICCVAM as a permanent committee. The Committee is composed of representatives from 15 Federal regulatory and research agencies; these agencies generate, use, or provide information from toxicity test methods for risk assessment purposes. The Committee coordinates cross-agency issues relating to development, validation, acceptance, and national/international harmonization of toxicological test methods.
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> The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) was established in 1998 to provide operational support for ICCVAM, and to carry out committee-related activities such as peer reviews and workshops for test methods of interest to Federal agencies. NICEATM and ICCVAM coordinate the scientific review of the validation status of proposed methods and provide recommendations regarding their usefulness to appropriate agencies. NICEATM and ICCVAM seek to promote the validation and regulatory acceptance of toxicological test methods that will enhance the agencies' ability to assess risks and make decisions, and methods that will refine, reduce, and/or replace animal use. The ultimate goal is the validation and regulatory acceptance of test methods that are more predictive of adverse

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[17] *EFED Review of Comments from Syngenta and its Contractors about the EPA Revised Environmental Risk Assessment for Atrazine, p. 22 (April 9 2002).* Attachment D.

> human and ecological effects than currently available methods. Such methods are expected to support improved protection of human health and the environment.[18]

ICCVAM has established a government-wide data quality standard that requires proper validation of tests before those tests can be considered reliable:

> Before a new or revised test method is used to generate information to support regulatory decisions, it must be (a) validated to determine its reliability and relevance for its proposed use, and (b) determined to be acceptable by one or more regulatory agencies to fill a specific need. Criteria for validation and regulatory acceptance have been prepared and are described in the report, *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the Ad Hoc Interagency Coordinating Committee on the Validation of Alternative Methods*. Prior to the initiation of any test method development or validation efforts, sponsors are encouraged to consider the validation and acceptance criteria developed by the Federal government.[19]

According to EPA and ICCVAM, validation is necessary to ensure reliable tests, and reproducibility is one of the primary scientific criteria for test validation:

> For a new or revised test method to be considered validated for regulatory risk assessment purposes, it should generally meet the following criteria....
>
> The extent of within-test variability, and the reproducibility of the test within and among laboratories must have been demonstrated. Data must be provided describing the level of intra- and interlaboratory reproducibility and how it varies over time. The degree to which biological variability affects this test reproducibility should also be addressed.[20]

EPA is a member of ICCVAM. EPA is one of the authors of the *Validation Guidelines* and *Validation Criteria* that established the government-wide validation requirement for test reliability and

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[18] http://iccvam.niehs.nih.gov/about/overview.htm

[19] Attachment B, *p. v (Validation Guidelines).*

[20] *Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods ("Validation Criteria")*, "Executive Summary", p. 2, Prepared by ICCVAM and NICEATM (March1997). Attachment E.

reproducibility.[21] Thus, according to EPA's own data quality standards, there is no reliable and reproducible information regarding atrazine's endocine effects because there are no validated tests for those effects.

V. EPA'S ENDOCRINE-EFFECTS STATEMENTS IN ITS *ENVIRONMENTAL RISK ASSESSMENT* VIOLATE THE DATA QUALITY ACT'S OBJECTIVITY, REPRODUCIBILITY, AND UTILITY STANDARDS BECAUSE THOSE STATEMENTS ARE NOT BASED ON VALIDATED TESTS

EPA's *Environmental Risk Assessment* continues to be disseminated to the public through EPA's public docket; through *Federal Register* notices; and through EPA's website. The *Environmental Risk Assessment* will form part of the basis for EPA's atrazine IREDs. Consequently, EPA's endocrine effects statements in the *Environmental Risk Assessment* are disseminations of information subject to the Data Quality Act Standards and Guidelines.[22]

EPA has stated that there are no validated tests for atrazine's endocrine effects. The Data Quality Act's Objectivity Standard requires "reliable" information.[23] EPA's statements about atrazine's endocrine effects in the *Environmental Risk Assessment* violate this standard because those statements are based on studies using unvalidated test methods. Until and unless there are properly validated tests, there can be no reliable information regarding atrazine's endocrine effects.[24]

Under EPA's Data Quality Guidelines, pages 19-20, the *Environmental Risk Assessment's* statements regarding atrazine's endocrine effects are Influential Scientific Information because:

- While final, EPA's *Environmental Risk Assessment* is by court order scheduled for further peer review by the Science Advisory Panel ("SAP") on the endocrine effects issue in the Spring of 2003[25];

- The atrazine endocrine-effects issue is controversial and precedent-setting[26]; and

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[21] Attachment B (*Validation Guidelines*), p. iii; Attachment E (*Validation Criteria*), "Agency Representatives and Participants," p. 1.

[22] EPA Guidelines, pp. 15-18; 67 FR 8460 (OMB Guidelines).

[23] 67 FR 8453, 8459 (OMB Guidelines); EPA Guidelines, p. 15.

[24] Attachment B, p. v *(Validation Guidelines*).

[25] Attachment C.

[26] Attachment F.

- NRDC has petitioned EPA to ban atrazine, one of the world's most widely used herbicides, based in part on these alleged endocrine effects[27].

For Influential Scientific Information like this, EPA's Data Quality Guidelines require that EPA "ensure reproducibility for disseminated original and supporting data according to commonly accepted scientific, financial, or statistical methods."[28] There are "commonly accepted scientific...methods" for ensuring reproducibility of new and revised tests: the ICCVAM *Validation Guidelines* and *Validation Criteria*. EPA cannot ensure reproducibility of original and supporting data until and unless that data is generated by reliable tests. Under government-wide data quality standards, proper test validation is necessary to demonstrate reproducibility.[29]

The need for endocrine effects test validation is evinced by the controversy over Dr. Hayes' frog studies. The Atrazine Ecorisk Panel has not been able to reproduce Dr. Hayes' test results.[30] Dr. Hayes and the Atrazine Ecorisk Panel do not even agree on how to test atrazine for endocrine effects on frogs.[31] This disagreement, and whether atrazine causes endocrine effects, can only be resolved through proper test validation.

The need for endocrine effects test validation is further evinced by the fact that Dr. Hayes has killed and continues to kill thousands of frogs in unvalidated tests that have no proven value.

EPA's statements regarding atrazine's endocrine effects also violate the Data Quality Act's Utility Standard. This Standard requires that information disseminated by EPA be useful to its intended users, including the public.[32] Information that is unreliable because it is generated from unvalidated tests is not useful.

In sum, the FQPA requires that EPA only use validated tests to assess human endocrine effects.[33] The Data Quality Act's Objectivity, Reproducibility, and Utility Standards require that EPA use validated tests to assess both human health and environmental endocrine effects.

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[27] Attachment G.

[28] EPA Guidelines, p. 47.

[29] Attachment E, pp. 2 (*Validation Criteria*).

[30] Attachment H.

[31] Attachments I and J.

[32] 67 FR 8459 (OMB Guidelines); EPA Guidelines, p. 15.

[33] 21 U.S.C. § 346a(p)(1).

VI. CRE AND THE TRIAZINE NETWORK ARE IMMEDIATELY AFFECTED PERSONS

The Triazine Network is a coalition of over 1000 local and state agricultural associations and farmers located throughout the United States.[34] It includes growers of various crops on which atrazine is used. The Triazine Network was established to respond to EPA's atrazine review. The Triazine Network commented extensively on EPA's atrazine review, raising the lack of test validation issue.[35] The Triazine Network's goal is to ensure an outcome to EPA's atrazine review based on sound science. The *Environmental Risk Assessment's* statements regarding atrazine's endocrine effects adversely affect this goal because they are not based on sound science.

Moreover, the *Environmental Risk Assessment* will ultimately form part of the basis of an IRED that will determine whether atrazine can continue to be used as a herbicide and under what conditions. An IRED based on unreliable EPA conclusions regarding atrazine's endocrine effects could adversely affect the ability of the Triazine Network's members to use atrazine.

This effect is immediate. The highly publicized controversy over atrazine and endocrine effects is impeding the Triazine Network's current and future ability to market, produce and use atrazine. EPA's *Environmental Risk Assessment's* statements regarding atrazine's endocrine effects fuel and encourage public misperceptions concerning atrazine. EPA's *Environmental Risk Assessment* must be corrected now in order to stop this flood of misinformation and bad science.

The Center for Regulatory Effectiveness has commented extensively on EPA's atrazine review. CRE continues to follow EPA's atrazine review on CRE's website, which now encompasses a section with its own domain, www.atrazine.us. The purpose of www.atrazine.us is to provide the public with accurate, scientifically valid information about atrazine. CRE's goal is adversely affected by the unreliable statements in the *Environmental Risk Assessment* regarding atrazine's endocrine effects.

CRE also has a long-standing and active interest in ensuring the quality of information disseminated by federal agencies. To achieve this goal, CRE actively advocated passage of the Data Quality Act. CRE has also commented on OMB's government-wide guidelines and on most agencies' proposed guidelines. CRE's website, TheCRE.com, contains extensive discussions of issues raised by OMB's government-wide guidelines and the agencies' proposed guidelines. CRE intends to continue its website coverage of and interest in the development and implementation of Data Quality Act guidelines, including agency action on Data Quality Act Requests for Correction.

Consequently, both the Triazine Network and CRE are "affected persons" for purposes of filing this Petition.[36]

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[34] Attachment K

[35] Attachment L, pp. 11-12.

[36] EPA Guidelines, pp. 30, 54; 66 FR 49721 (Sept. 28, 2001)(OMB's Interim Final Government-Wide Guidelines).

VII. CORRECTION REQUESTED

As soon as possible, EPA should correct its *Environmental Risk Assessment* at pages 11, 90-94, to state that there is no reliable evidence that atrazine causes "endocrine effects" in amphibians, fish, mammals or any other kind of animal. EPA's corrected *Environmental Risk Assessment* should state that there can be no reliable, accurate or useful information regarding atrazine's endocrine effects until and unless there are test methods for those effects that have been properly validated.

Please contact Jim Tozzi at the Center for Regulatory Effectiveness with respect to this Request for Correction.

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