PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

PETA

PCRM PHYSICIANS COMMITTEE FOR RESPONSIBLE MEDICINE

PETITION TO COMPEL THE U.S. EPA TO LIMIT THE SCOPE OF ITS ENDOCRINE DISRUPTOR SCREENING PROGRAM TO EFFECTS IN HUMANS GIVEN ITS CHRONIC FAILURE TO MEET STATUTORY DEADLINES FOR PROGRAM IMPLEMENTATION

January 4, 2005

SUBMITTED TO

The U.S. Environmental Protection Agency

SUBMITTED BY

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VIA MAIL AND ELECTRONIC TRANSMISSION: Leavitt.Michael@epa.gov

The Honorable Michael Leavitt
Administrator
U.S. Environmental Protection Agency
Ariel Rios Bldg. (1101A)
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

RE: PETITION FOR RULEMAKING TO COMPEL THE U.S. EPA TO LIMIT THE SCOPE OF ITS ENDOCRINE DISRUPTOR SCREENING PROGRAM TO EFFECTS IN HUMANS GIVEN ITS CHRONIC FAILURE TO MEET STATUTORY DEADLINES FOR PROGRAM IMPLEMENTATION

Dear Administrator Leavitt:

On behalf of the more than 800,000 members of People for the Ethical Treatment of Animals (PETA), the 5,000 physician and more than 100,000 lay members of the Physicians Committee for Responsible Medicine (PCRM), and a coalition of national animal and environmental protection organizations with a combined membership of more than 10 million Americans, we hereby petition the U.S. Environmental Protection Agency (EPA) to limit the scope of its Endocrine Disruptor Screening Program (EDSP) to determining whether "certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate." 21 *U.S.C.* §346a(p). This petition for rulemaking is submitted pursuant to the Administrative Procedure Act (APA), 5 *U.S.C.* §553(e).

FACTUAL BACKGROUND

The Food Quality Protection Act of 1996 (FQPA), 21 *U.S.C.* §346a, *et seq.* amended both the Federal Insecticide Fungicide and Rodenticide Act (FIFRA), 7 *U.S.C.* §136a, and the Federal Food, Drug, and Cosmetics Act (FFDCA), 21 *U.S.C.* §301. Under the FQPA, the EPA must make a determination as to whether pesticide residues remaining in or on food are "safe." 21 *U.S.C.* §346a(b)(2)(A)(i). Accordingly, the EPA must complete a comprehensive assessment of each pesticide's risks to humans considering aggregate exposure from food, drinking water, and residential uses, as well as the cumulative effects for all pesticides sharing a common mechanism of toxicity. 21 *U.S.C.* §346a(b)(2)(D).

The Safe Drinking Water Act (SDWA), 42 *U.S.C.* §300j-17, similarly provides the EPA with authority to require testing of any substance that might be found in sources of drinking water if the Agency determines that a substantial population might be exposed to the substance.

The FQPA contains specific provisions relating to the potential for the increased susceptibility of infants and children. Specifically, the statute requires the EPA to assess the risk of pesticide chemical residue based on:

> [T]he special susceptibility of infants and children to the pesticide chemical residues, including neurological differences between infants and children and adults, and effects of *in utero* exposure to pesticide chemicals.

21 *U.S.C* §346a(b)(2)(C)(i)(II).

Among the factors the EPA must consider with respect to pesticide tolerances, is whether the pesticide "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate." 21 *U.S.C.* §346a(b)(2)(D)(viii). This is the first of six references in the statute to endocrine effects "in humans." This same language appears five additional times in five discrete provisions of the law.

The second section of the FQPA to reference endocrine effects in humans is 21 *U.S.C.* §346a(d)(2)(A)(x). Under that section, any person may file a petition with the Agency seeking the issuance of a regulation concerning tolerances and exemptions. A petition to establish either a tolerance or an exemption must be supported by *inter alia,* "such information as the Administrator may require on whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects…"

The third FQPA Section, §346a(f)(1)(C), empowers the Agency to require additional data about a pesticide, including "whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects."

The fourth reference to endocrine effects in humans is the section in which Congress mandated the development and implementation of the Estrogenic Substances Screening Program. That provision of the statute reads as follows:

> (1) Development. – Not later than 2 years after the date of enactment of this section, the Administrator shall in consultation with the Secretary of Health and Human Services, develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate.

21 U.S.C. §346a(p)(1).

The fifth and sixth references to endocrine effects in humans appear in 21 *U.S.C.* §§346a(p)(4) and (6). Subsection (4) permits the EPA to exempt a pesticide from the EDSP if "the substance is anticipated not to produce any effect in humans similar to an effect produced by a naturally occurring estrogen." Subsection (6) authorizes the Agency to take action to protect the public health in cases where a substance is found "to have an endocrine effect on humans …""

In sum, the FQPA contains six specific references to endocrine effects in humans, each using nearly identical language, each referring exclusively to endocrine effects in humans, and

each unambiguously clear. That Congress intended the EDSP to be limited to endocrine effects **in humans** is beyond peradventure.

It is equally clear that Congress directed that the EDSP be developed using validated test systems "[n]ot later than 2 years" after the date of enactment, and implemented "[n]ot later than 3 years" after the date of enactment. The EPA has met neither of these deadlines, thus violating its non-discretionary duties under §§346a(p)(1) and (2) of the FQPA.

UNAUTHORIZED EXPANSION OF THE SCOPE OF THE EDSP TO INCLUDE ASSESSMENT OF ECOLOGICAL EFFECTS

Following enactment of the FQPA, the EPA established the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) and charged the Committee with "providing advice to the Agency on how to design a screening and testing program for endocrine disrupting chemicals" (EDSTAC, 1998, p. 1 – 2). Moreover:

> In convening the EDSTAC, EPA did not limit the Committee to the narrow set of chemicals and the single hormonal system explicitly mentioned in the FQPA and SDWA [Safe Drinking Water Act] endocrine disruptor screening and testing provisions. Nor did the EDSTAC limit its recommendations to the protection of human health. Rather… the EDSTAC strongly recommends that EPA's endocrine disruptor screening and testing program should:
>
> - address both human health and ecological effects;
> - initially emphasize identifying and characterizing effects that enhance, mimic, or inhibit estrogen, androgen, and thyroid hormone-related processes; and
> - be capable of evaluating the endocrine disrupting properties of both chemical substances and common mixtures.
>
> (EDSTAC, 1998, p. 2 – 6).

EDSTAC's *Final Report* established the present-day architecture of the EDSP. Following EDSTAC's recommendation, the Agency formally expanded the scope of the EDSP to assess ecological effects in multiple taxonomic groups, including birds, fish, amphibians, and invertebrates (63 Fed. Reg. 71542, 71550-58, 28 Dec. 1998).[1] The Agency did this in clear disregard of the plain language of the FQPA, which specifies on six separate occasions, that the focus of the EDSP is to be on endocrine effects "in humans."

[1] The following documents, which appear on the Agency's website (EPA, 2004b), further document the EPA's expansion of the EDSP to the assessment of ecological effects in multiple taxonomic groups:

- Keystone Convening Report relating to the formation of EDSTAC.
- *Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) Final Report*.
- Draft Detailed Review Papers on Fish Screening Assays; on Comparative Evaluation of Vitellogenin Methods; and on A Fish Two-Generation Toxicity Test.
- Draft Final Reports on Comparative Evaluation of Fathead Minnow Assays; and on Comparative Evaluation of Vitellogenin Methods.
- Draft Study Plan on Comparative Evaluation of Vitellogenin Methods; on Avian Dosing Study; and on Comparative Evaluation of Fathead Minnow Assays.
- Revised Draft Detailed Review Paper for Amphibian Metamorphosis Assay; for Avian Two-Generation Toxicity Test; and for Mysid Life Cycle Toxicity Test.
- Draft Proposal for a New Guideline for Fish Two-Generation Test Guideline.

The statutory language mandating the development of the EDSP imposed no legal obligation on the EPA to determine the effects of substances on species other than humans. Indeed, the unambiguous language of the FQPA reflects the clear intent of Congress that the focus of the EDSP was to be on endocrine effects "in humans."

The relevant legal inquiry on statutory construction wholly supports this petition. The case of *Safe Food and Fertilizer v. EPA*, 350 F. 3d 1263, 1267 (D.C. Cir. 2004) is instructive. In that case, the Court observed that, "unless the [plain language of the] statute resolves the issue, we must uphold the EPA so long as its interpretation is reasonable." In the first instance, as fully described above, the plain language of the statute limits the EDSP to a screening and testing program for estrogenic or other endocrine effects **in humans**. Accordingly, whether the EPA's broadening the EDSP to include wildlife is a reasonable interpretation of the statute should rise or fall on the plain words of the Act.

Even if the judiciary were to consider the reasonableness of the EPA's interpretation of the FQPA, the outcome would be the same. Courts employ a doctrine known as *ejusdem generis* in determining the scope of a statute. The *ejusdem generis* rule is that where general words follow an enumeration of particular and specific words, the general words are to be construed narrowly as applying only to those classes of persons or things specifically mentioned. *Black's Law Dictionary* 464 (5th ed. 1979). The *ejusdem generis* cannon and its sister maxim known as *noscitur a sociis*, were expounded upon in detail in the case of *Williams v. Hot Shoppes, Inc.*, 293 F. 2d 835, 850 (D.C. Cir. 1961):

> When a particular class of persons or things is spoken of in a statute and general words follow, the class first mentioned must be taken as the most comprehensive, and the general words treated as referring to matters *ejusdem generis* with such class, the effect of general words when they follow particular words being thus restricted. Things exceptional in character are never legally deemed to be included or embraced in general terms of disposition, prohibition or regulation of a class or classes of normal or ordinary subjects mentioned. This principle is the basis or meaning of the rule *ejusdem generis*.
>
> It is a fundamental rule of construction that in accordance with the maxim *noscitur a sociis* the meaning of a word or phrase may be ascertained by reference to the meaning of other words or phrases with which it is associated. Language, though apparently general, may be limited in its operation or effect where it may be gathered from the intent and purpose of the statute that it was designed to apply only to certain persons or things, or was to operate only under certain conditions.
>
> In the interpretation of statutes, words and phrases therein are often limited in meaning and effect by necessary implications arising from other words or clauses thereof.

The operative words here are whether "certain substances may have an effect **in humans** that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate." 21 *U.S.C.* §346a(p). By applying the *ejusdem generis* rule, the persons or things named in the statute are exclusively "humans"—not wildlife or other animals. The testing is for estrogenic effects "or such other endocrine effect" as the EPA may designate. Those words of general application are limited in two ways: they must

be endocrine-related effects and they must be applied to "humans."[2] *See also*, *Van EE v. EPA*, 202 F.3d 296, 302 (D.C. Cir. 2000)(Subsequent terms under canon of *ejusdem generis* must share the same attributes as the preceding terms.); *Cole v. Burns International*, 105 F. 3d 1465, 1471 (D.C. Cir. 1997)(General phrase takes its meaning from specific terms preceding it.); and *U.S. v. Thomas*, 361 F.3d 653, 659 (D.C. Cir. 2004) (When a statute begins with a specific category and ends with a general catch-all, the canons of *ejusdem generis* and *noscitur a sociis* counsel that the latter be read in light of the former.)

The foregoing notwithstanding, the parties to this submission are well aware of the various other statutory authorities under which the EPA is capable of requiring testing (e.g., FIFRA, TSCA, etc.). However, these authorities are separate and distinct from the limited Congressional mandate given the Agency under the FQPA, and in no way provide a lawful excuse for the EPA's chronic failure to meet even its minimal, non-discretionary duties under the FQPA.

EPA'S FAILURE TO MEET ITS CONGRESSIONALLY MANDATED DEADLINES IS A DIRECT RESULT OF ITS EXPANSION OF THE EDSP TO INCLUDE ASSESSMENT OF ECOLOGICAL EFFECTS IN MULTIPLE TAXONOMIC GROUPS

The FQPA requires that, "Not later than 2 years after the date of enactment of this section, the Administrator shall … develop a screening program…." 21 *U.S.C.* §346a(p)(1). The Act further stipulates that, "Not later than 3 years after the date of enactment of this section, after obtaining public comment and review of the screening program described in paragraph (1) … the Administrator shall implement the program." 21 *U.S.C.* §346a(p)(2). In practical terms, the EDSP was to have been "developed" by August 3, 1998, and "implemented" by August 3, 1999. The EPA has failed to meet either of these explicit statutory deadlines,[3] and is now more than five years behind schedule in implementing the EDSP.

As a result of the EPA's failure to implement the EDSP by the August 1999 deadline, the Natural Resources Defense Council (NRDC) sought declaratory judgment that the EPA had unlawfully withheld Agency action and failed to perform a nondiscretionary duty under the FFDCA §408(p) to implement the EDSP in accordance with its statutory deadline, and a preliminary and permanent injunction ordering the EPA to expeditiously implement the Program. On January 19, 2001, the NRDC and the EPA signed a Settlement Agreement, under which the EPA agreed to "use best efforts" to:

- complete development of the architecture of the Endocrine Disruptor Priority Setting Database by **July 31, 2001**.
- complete and validate the Quantitative Structure-Activity Relationship (QSAR) portion of the EDPSD by **December 31, 2001**.
- ensure that the EDPSD will be operational by **May 31, 2002**.
- complete Validation of all of the Tier 1 screens except the Frog Thyroid assay no later than **December 31, 2003**.
- complete validation of the Frog Thyroid assay. EPA will determine whether to include the Frog Thyroid assay as part of Tier 1 by **December 21, 2002**.
- complete validation of the *in utero* lactation assay no later than **December 31, 2003**.

[2] The EPA's expansion of the EDSP to screen for androgenic and thyroid effects is not under dispute, as consideration of such "other endocrine effects" as they pertain to humans is clearly permitted under the statutory language of the FQPA.
[3] The EPA could argue that it has met the August 1998 deadline in the sense that a detailed program was proposed and published in the Federal Register (63 Fed. Reg. 42852, 11 Aug. 1998; 63 Fed. Reg. 71542, 71550-58, 28 Dec. 1998); however, the Agency has yet to fully validate even one of the proposed screens or tests, nor has it determined the final composition of the Tier 1 screening battery.

- complete Validation of the Tier 2 Mammalian Two-generation Assay no later than **December 31, 2004**.
- start requiring testing, using appropriate regulatory mechanisms, for certain Tier 1 screens…no later than **December 31, 2003**.
- start requiring testing, using appropriate regulatory mechanisms, for certain Tier 2 tests…no later than **December 31, 2004**.

The Settlement Agreement also stipulated that the "EPA will endeavor to (1) reduce the number of animals used in implementing the Endocrine Disruptor Screening Program (EDSP), (2) refine procedures to make animal tests used in the Program less painful or stressful, and (3) replace animals with non-animal systems, where scientifically appropriate."

The EPA has failed to meet virtually all of the agreed-upon deadlines under this Settlement Agreement. In fact, most of the screens and tests under development are not even close to being validated or suitable for routine use, as is evident from the progress reports posted on the Agency's website (EPA, 2004b). The EPA's chronic failure to fulfill even its minimal non-discretionary duties under the FQPA (i.e., implementing an **Estrogenic** Substances Screening Program to evaluate chemical effects **in humans**)—or to meet any of the generous extensions specified and agreed to in the NRDC Settlement—is directly attributable to the Agency's voluntary, unnecessary, and unauthorized expansion of the EDSP to assess endocrine effects in species other than humans. PETA has repeatedly brought this fact to the Agency's attention—most recently in public comments dated March 19, 2003 (attached as Exhibit 1) and August 20, 2003 (attached as Exhibit 2).

According to the Agency's website (EPA, 2004a):

> EPA is currently developing and validating approximately 14 assays, the majority of which are being considered for the Tier 1 Screening battery. Tier 1 Screening is designed to detect chemical substances capable of interacting with the estrogen, androgen, and thyroid hormonal systems. Once all of the Tier 1 Screening assays are validated, EPA with stakeholder and public input will propose a battery of screens for peer review. Tier 2 Testing is designed to determine whether a chemical may have an effect similar to that of naturally occurring hormones and to identify, characterize, and quantify those effects for estrogen, androgen, and thyroid hormones.

Screening and testing methods currently under development and validation by the EPA include:

Tier 1 Screens	Tier 2 Tests
Amphibian Metamorphosis	Amphibian 2-Generation
Androgen Receptor (AR) Binding	Avian 2-Generation
Aromatase	Fish Lifecycle
Estrogen Receptor (ER) Binding	Invertebrate Lifecycle
Fish Screen	Mammalian 2-Generation
Hershberger	
Pubertal Female	**Tier to be determined**
Pubertal Male	In Utero through Lactation
Steroidogenesis	

Had the EPA adhered to the plain language of the FQPA—i.e., determining estrogenic or other endocrine effects in humans—the number of screens and tests requiring development and validation could be reduced to eight or fewer (AR and ER Binding, Aromatase, Hershberger, Pubertal Male or Female, Steroidogenesis, and/or Mammalian 2-Generation). And had the EPA limited the scope of the EDSP to strictly estrogenic effects in humans, the number of screens and tests could be further reduced to three or fewer (ER binding and/or Pubertal Female and/or Mammalian 2-Generation). Arguably, either scenario could have been manageable for the EPA, although the latter could most easily have been implemented within the three-year timeframe mandated by Congress.

However, with each step the EPA has taken to expand the scope of the EDSP, the Agency has fallen farther behind schedule in terms of timely implementation of the EDSP. Nowhere is this more evident than in the EPA's addition of ecotoxicological assessments in multiple taxonomic groups. This move alone added six large and highly complex studies to the EPA's workload. Whereas the proposed Tier 1 screens (amphibian metamorphosis and fish screen) would consume an estimated 30 frogs and 60 fish, respectively (Purchase, 2003), the 2-generation and lifecycle tests under development for Tier 2 can consume thousands of animals[4] and take weeks or months to conduct, at a cost of hundreds of thousands of dollars (Derelanko & Hollinger, 2002, p. 1327).[5]

Adding to the complexity of the EPA's task is the further FQPA requirement that the EDSP be based on the use of "appropriate validated test systems…." 21 *U.S.C.* §346a(p). Validation is "the process by which the reliability and relevance of a procedure are established for a particular purpose" (ICCVAM, 2003). A formal validation study is a costly undertaking, which generally involves several participating laboratories testing of a pre-determined slate of chemicals using the same, standardized protocol. A valid test should produce consistent results both between and within laboratories, and be a demonstrably relevant predictor of effects in the species of ultimate interest (ICCVAM, 2003). Validation studies can take months or years to complete for even a relatively rapid and inexpensive cell culture study, to say nothing of an already lengthy and highly complex multi-generational reproduction study (Worth & Balls, 2002, p. 17, attached as Exhibit 3). Yet the EPA has committed itself to developing and validating not just one 2-generation/lifecycle study, but five such studies, in five distinct taxonomic groups.

It does not require a quantum leap to deduce that the EPA's voluntary expansion of the EDSP to include ecotoxicity studies in multiple taxonomic groups is the root of the Agency's more than five-year delay in implementing the EDSP in accordance with the deadlines set by Congress. It should also go without saying that compliance with a Congressional mandate should take precedence over agency- and stakeholder-proposed tangents. Yet in the case of the EDSP, the opposite situation has emerged: EDSTAC recommended the marked expansion of the Program to include nearly a dozen superfluous screening and testing methods for several hormone types in multiple taxonomic groups, and the EPA embraced this recommendation wholeheartedly. In so doing, the Agency has created a program that is so large and unwieldy in its scope and costs that timely implementation has become a virtual impossibility.

For these reasons, we respectfully urge the Administrator to grant this petition and limit the scope of the EDSP to endocrine effects in humans.

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[4] On the basis of Agency Test Guidelines (EPA, 1998) and study designs outlined in draft Detailed Review Papers (EPA, 2003; Purchase, 2003; Fischer, 2003), 2-generation reproduction studies could consume 2,500 or more rats and 5,500 or more birds per chemical studied.

[5] The *Handbook of Toxicology* (Derelanko & Hollinger, 2002, p. 1327) reports the typical cost of a 2-generation reproduction study in rats to be $300,000. Other Tier 2 tests under development may be more or less costly, depending on the species and number of animals involved and other factors.

ADDITIONAL STATUTORY MANDATES

There are additional points we ask the Administrator to consider in conjunction with the expansion of the EDSP. Those are the public policy considerations expressed in the ICCVAM Authorization Act, 42 *U.S.C.* §2851 *et seq*., and the National Institutes of Health Revitalization Act of 1993, 42 *U.S.C.* §283e. Each Act expresses Congressional intent with respect to the reduction, refinement, and ultimate replacement of animal use in testing. Each Act positively supports the merits of this petition, since the expansion of the EDSP to include testing for endocrine effects in other taxonomic groups not only fosters continued reliance on animal-based methods, but could more than quadruple the amount of animal testing that takes place, in the event that all five of the Tier 2 multi-generation/lifecycle tests were to be required.

One of the central aims of the ICCVAM Authorization Act is to promote and advance alternatives to animal-based testing. In establishing ICCVAM as a permanent Committee, Congress signaled its firm commitment to the advancement of *in vitro* and other non-animal-based testing methods. ICCVAM's mandate is clear: new and revised test methods are to be scientifically validated, and reliance on animal-based methods must be reduced, refined and replaced.

Similarly, the NIH Revitalization Act of 1993 directs the National Institutes of Health to conduct or support research into methods of research that "do not require the use of animals," that "reduce the number of animals used in such research," that encourage the "acceptance by the scientific community" of alternative methods, and that trains "scientists in the use of such methods." 42 *U.S.C.* §283e.

The expansion of the EDSP to include ecological effects stands in sharp counterpoise to the principles espoused in the ICCVAM Authorization Act and the NIH Revitalization Act.

CONCLUSION

For the foregoing reasons, we respectfully urge the Administrator to initiate rulemaking restricting the scope of the EDSP to the determination of endocrine effects in humans in compliance with the FQPA, and to adhere to the deadlines mandated therein.

We would appreciate your immediate attention to this petition, and will anticipate receiving the Agency's response within a "reasonably prompt time," as required by the APA.

Respectfully submitted,

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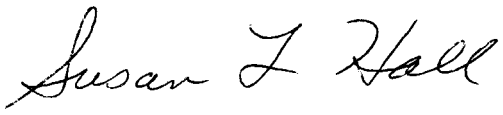

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