February 11, 2008

Dr. William Wooge
Office of Science Coordination and Policy (7201M)
Environmental Protection Agency
1200 Pennsylvania Ave. N.W.
Washington, DC 20460-0001

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

HEADQUARTERS
501 FRONT STREET
NORFOLK, VA 23510
TEL 757-622-PETA
FAX 757-622-0457

Re: **72 FR 33486, June 18, 2007, Docket ID number EPA-HQ-OPPT-2004-0109; Draft List of Initial Pesticide Active Ingredients and Pesticide Inerts to be Considered for Screening under the Federal Food, Drug and Cosmetic Act.**

Dear Dr. Wooge:

These comments are submitted on behalf of the Alternatives Research and Development Foundation, the American Anti-Vivisection Society, Earth Island Institute, the Humane Society Legislative Fund, The Humane Society of the United States, the People for the Ethical Treatment of Animals and the Physicians Committee for Responsible Medicine. The parties to this submission are national animal protection, health, and scientific advocacy organizations with a combined constituency of more than 10 million Americans who share the common goal of promoting reliable and relevant regulatory testing methods and strategies that protect human health and the environment while reducing, and ultimately eliminating, the use of animals.

The Environmental Protection Agency (EPA) is requesting comments regarding the draft list of initial chemicals to be tested in the EPA's Endocrine Disruptor Screening Program (EDSP). This list consists of 73 chemicals including 64 pesticide active ingredients and nine high production volume (HPV) inert ingredients. The selection of chemicals was based entirely on exposure potential without regard to potential activity. Several if not most of the compounds on this list have been well characterized with regard to toxicity, including some endocrine-related endpoints; therefore, to require further endocrine-related testing would result in needless duplication and waste of resources and cause immense animal suffering and death.

Pesticides are among the most highly data-rich substances in existence. For registration, pesticides currently are often subject to dozens of separate animal tests, including, reproductive and chronic/lifecycle studies in rodents, fish and birds.[1] These tests kill thousands of animals and include many of the same endpoints addressed in the presumptive EDSP Tier 2 tests. Similarly, US EPA's Chemical Challenge Program also provides for the collection of data which may be germane to the assessment of potential reproductive toxicity.[2] At an absolute minimum, chemicals should be exempted from EDSP Tier 1 screens for which equivalent or higher tier data are available.

[1] 72 FR 60934, October 26, 2007: EPA 40 CFR Parts 9 and 158: Pesticides; Data Requirements for Conventional Chemicals.
[2] 65 FR 81657, December 26, 2000; EPA 40 CFR Part 799: Testing of Certain High Production Volume Chemicals

Following this reasoning, testing requirements should be tailored to individual chemicals and/or chemical classes. For example, Reproduction and Fertility effects (OPPTS 870.3880) and Prenatal Developmental Toxicity (OPPTS 870.3700) tests are required for both food-use and non-food-use pesticide Technical Grade of the Active Ingredients (TGAI). The simple mechanistic data produced by the Hershberger, Uterotrophic, the male and female pubertal assays will not provide additional information; indeed, chemicals tested according to OPPTS 870.3880 have, in effect, already been subject to EDSP Tier 2 mammalian testing. Thus, with the possible exception of mechanistic screening for thyroid effects, EDSP Tier 1 screens would appear to provide little or no value-added for pesticide chemicals.

In addition, four of the chemicals included on this draft list (atrazine, butylbenzyl phthalate, di-*n*-butyl phthalate and linuron) are included in the Revised ICCVAM List of Recommended ED Reference Substances. Atrazine has been well characterized in terms of its endocrine activity in numerous *in vitro* and *in vivo studies*, including *in vivo* studies and risk assessments already conducted by the EPA.[3] In fact, the use of atrazine has been prohibited in Europe due to its endocrine activity.[4] Similarly, butyl benzyl phthalate (BBP) has been shown to possess endocrine activity in *vitro* and *in vivo* in numerous animal studies, including those already conducted by the EPA.[5,6]

The anti-androgenic activity of di-*n*-butyl phthalate (DBP) has been studied in detail.[7,8] Both BBP and DBP have been associated with endocrine-related effects in humans.[9] Linuron is a well-characterized weak anti-androgen, and was used as a control in OECD validation exercises for the Hershberger assay[10,11] and as a control in the EPA's own evaluation of the 15-day intact male assay.[12] Due to the abundance of existing endocrine-related data, it is unlikely that further testing using the presumptive Tier 1 or Tier 2 EDSP assays will provide any additional information regarding the endocrine activity of these chemicals. Therefore, at a minimum, these four chemicals should also be removed from the draft list.

Regardless of the amount of endocrine-relevant information that may be available for some of these compounds, it appears, from this notice and comments made at the EPA's Public Workshop

[3] Gammon, D.W, et al., 2005. A risk assessment of Atrazine use in California: human health and ecological aspects. Pest. Manag. Sci. 61: 331-55.
[4] Sass and Colangelo, 2006. European Union bans Atrazine, while the United states negotiates continued use. Int. J. Occup. Environ. Health. 12:260-7.
[5] Gray, et al., 2000. Perinatal exposure to the phthalates DEHP, BBP and DINP, but no DEP, DMP, or DOTP alters sexual differentiation I of the male rat. Toxicol. Sci. 58: 350-65
[6] Aso, et al., 2005. A two-generation reproductive toxicity study of butyl benzyl phthalate in rats. J. Toxicol. Sci. 30 Spec No.:39-58.
[7] Bredhult, C. et al., 2007. Effects of some endocrine disruptors on the proliferation and viability of human endometrial endothelial cells. Reprod. Toxicol. 23:550-9.
[8] Wang Y.B., et al. 2007 Monobutyl phthalate inhibits steroidogenesis by down-regulating steroidogenic acute regulatory protein expression in mouse Leydic tumor cells (MLTC-1). Toxicol. Environ, Health. A. 70:947-55.
[9] Marsee, K. et al., 2006. Estimated daily phthalate exposures in a population of mothers of male infants exhibiting reduced anogenital distance. Environ. Health. Perspect. 114: 805-9.
[10] Owens, et al., 2007. The OECD program to validate the rat Hershberger bioassay to screen compounds for in vivo androgen and anti-androgen responses: phase 2 dose-response studies. Environ. Health. Perspect. 115:671-8.
[11] Tinwell, H., et al., 2007. Evaluation of the anti-androgenic effects of flutamide, dDE, and Linuron in the weanling rat assay using organ weight, hispathological and proteomic approaches. Toxicol. Sci. 100:54-65.
[12] http://www.epa.gov/scipoly/oscpendo/pubs/adult_male_peer_review_final.pdf

on the EDSP; Policies and Procedures for initial screening, December 17, 2007, that the EPA intends to test all 73 chemicals in all Tier 1 screens which have yet to be determined. Further, it is not at all clear how mechanistic screening data will influence the regulation of substances that have already been subject to extensive apical testing and complete human health and ecotoxicological risk assessments.

The EPA states that "the ultimate purpose of the EDSP is to provide information to the Agency that will allow the Agency to evaluate the risks associated with the use of a chemical and take the appropriate steps to mitigate any risks." A major difficulty in assessing this draft list of initial compounds for testing is that many of the elements have not yet been defined. For example, since neither the assays nor testing batteries to be included in the EDSP have been finalized, it's not clear exactly what data will be generated either by Tier 1 or Tier 2 testing. Nor has the EPA provided any explanation as to how EDSP data will be used to assess risk (or reassess, in the cases where risk assessments have already been done), either to human health or the environment. Nor has there been any explanation from the EPA regarding the "steps" that might be taken to mitigate these risks.

In this notice, the EPA is asking stakeholders and the public to evaluate a list of compounds as to their appropriateness for use in a testing scheme that is largely undefined. One therefore is left to make some profound assumptions in order to evaluate whether this list of compounds is appropriate. One is also left with the perception that the EPA is hastily piecing together a testing program that is based largely on expedience rather than on a sound regulatory decision making process. There can be no justification whatsoever for subjecting animals to such immense suffering for what is simply an ill-conceived exploratory exercise.

Thank you for considering our comments.

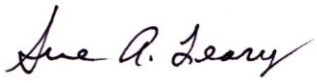
Sincerely,

Catherine Willett, PhD
Science Policy Advisor
Regulatory Testing Division
People for the Ethical Treatment of Animals

Troy Seidle
Science Policy Advisor
Humane Society of the United States

Dr. Martin Stephens
Vice President for Animal Research Issues
Humane Society of the United States

Kristie Stoick, MPH
Research Analyst
Physicians Committee for Responsible Medicine



Sue A. Leary
President
Alternatives Research & Development Foundation

Tracie Letterman, Esq.
Executive Director
American Anti-Vivisection Society