UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

PHYSICIANS COMMITTEE FOR RESPONSIBLE MEDICINE, 5100 Wisconsin Ave., N.W., Suite 400, Washington, DC 20016, **PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS,** 501 Front St., Norfolk, VA 23510, **TRULIE ANKERBERG-NOBIS,** 8322 Roanoke Ave., Takoma Park, MD 20912, **ROBIN HUMMEL,** 9134 Granby St., Norfolk, VA 23503 **JENNIFER REILLY,** 8102 Chester St., Takoma Park, MD 20912, Plaintiffs, v. **U.S. ENVIRONMENTAL PROTECTION AGENCY** and **STEPHEN L. JOHNSON,** Administrator, Environmental Protection Agency, 1200 Pennsylvania Ave., NW Washington, DC 20460, Defendants.	Civil Action No. **COMPLAINT**

Plaintiffs, by and through counsel, as and for their complaint herein, allege as follows, upon information and belief except as the allegations specific to the plaintiffs:

NATURE OF THE ACTION

1. This case challenges the U.S. Environmental Protection Agency's ("EPA" or "Agency") January 3, 2005 denial of Plaintiffs' petition requesting that the Agency repeal its Developmental Neurotoxicity Test Guidelines ("DNT Guidelines"). The methodology described in EPA's DNT Guidelines has never been subject to formal or adequate scientific validation to verify that the results of this animal test are reliable and relevant predictors of real-world effects in the species of concern (i.e., human beings). Notwithstanding the significant flaws in this test method, EPA is requiring DNT testing with ever increasing frequency (e.g., as a condition of registration and re-registration, and possibly as a new "conditional requirement" for all conventional pesticide chemicals (70 Fed. Reg. 12275, March 11, 2005)). Further, EPA has used DNT test results to justify allowing children (those in the womb, nursing infants, and growing children) to be exposed to pesticide levels many times higher than the statutory tenfold "children's health safety factor" established by Congress under the Food Quality Protection Act of 1996 ("FQPA")(PL 104-170, August 3, 1996, which in relevant part amended 21 U.S.C. § 346a).

2. Specifically, prior to enactment of the FQPA, the Federal Food, Drug, and Cosmetic Act at 21 U.S.C. § 346a required EPA to set tolerances for pesticides residues on food, but mandated no special treatment for infants and children. Congress enacted the FQPA in recognition of the fact that children (*in utero*, nursing, or at any stage before their nervous systems are fully developed) may be more susceptible than adults to chemical insult. Thus, as amended, § 346a(b)(2)(A)(i) provides that:

> The [EPA] Administrator may establish . . . a tolerance for a pesticide chemical residue in or on food only if the Administrator determines that the tolerance is safe.

§ 346a(b)(2)(C) provides that:

> Exposure of infants and children
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> In establishing, modifying, leaving in effect or revoking a tolerance or exemption from a pesticide chemical residue, the Administrator—
>
> (ii) shall—
> (I) ensure that there is a **reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue; and**
>
> * * *
>
> In the case of threshold effects, for purposes of clause (ii)(I) **an additional tenfold margin of safety for the pesticide chemical residue shall be applied for infants and children** to take into account potential pre- and post-natal toxicity and completeness of data with respect to exposure and toxicity to infants and children. Notwithstanding such requirements for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide residue only if, on the basis of reliable data, such margin will be safe for infants and children. [Emphasis supplied.]

The statute defines "safe" at 346a(b)(2)(ii):

> [T]he term "safe," . . . means the Administrator has determined that there is a **reasonable certainty that no harm will result** from aggregate exposure. [Emphasis supplied.]

3. Congress' mandate to EPA was to set exposure limits for children that were ten-times stricter (hereinafter the "Tenfold Safety Factor") than adult levels, unless the Agency could determine to a "**reasonable certainty that no harm will result**." In practice, EPA has used the DNT and the results of other non-validated animal tests to set pesticide tolerances and other permissible exposure levels for children that are marginally or no safer than the adult standard. For example, the August 6, 1998 "*Combined Report of the Hazard Identification Assessment*

Review Committee and the FQPA Safety Factor Committee" (HIARC/FQPA SFC) recommended, with respect to 40 organophosphate pesticides, that the Tenfold Safety Factor be removed entirely for 18 substances, retained for 12 substances, and reduced to three-fold for 10 substances. EPA takes these actions though it is well aware that DNT testing barely qualifies as "scientific," and is fraught with so many uncertainties and problems that its use to establish "reasonable certainty" is, beyond reasonable dispute, arbitrary, and capricious.

4. The DNT Guidelines and the data gathered through their use are inextricably linked to EPA's decision making in connection with the Tenfold Safety Factor. EPA has taken the position that unless DNT testing is performed for a selected chemical, a "gap" exists in the toxicity database and the Agency will apply the Tenfold Safety Factor (i.e., "the uncertainty related to the absence of a developmental neurotoxicity study makes it appropriate to apply a FQPA safety factor for acute and chronic dietary and non-dietary risk assessments for the general population including infants and children" (HIARC/FQPA SFC, 1998)). Thus, in the absence of the DNT Guidelines, EPA would require compliance with the FQPA.

5. The DNT Guidelines as employed by EPA expose America's children to substantially higher levels of pesticides—and potentially increased health risks—than Congress intended when enacting the FQPA. Since the DNT Guidelines have not been proven to reliably predict developmental neurotoxicity in humans, EPA is, in truth and in fact, allowing adverse developmental outcomes to be identified through chemical exposure to human children. This is unacceptable—particularly in light of the National Research Council's (NRC) recent finding that "3% of developmental disabilities are the direct consequence of neurotoxic environmental exposures, and that another 25% arise out of the interplay of environmental factors and

individual genetic susceptibility" (NRC. *Scientific Frontiers in Developmental Toxicology and Risk Assessment.* Washington, DC: National Academy Press (2000)).

6. EPA's denial of Plaintiffs' petition to repeal the DNT Guidelines violated the Administrative Procedure Act ("APA"), 5 U.S.C. § 706, as that decision was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law.

JURISDICTION AND VENUE

7. This Court has jurisdiction pursuant to 28 U.S.C. § 1331 and the APA, 5 U.S.C. §§ 701-706.

8. Venue is proper under 28 U.S.C. § 1391(e) in that EPA and its Administrator are headquartered in the District of Columbia.

PARTIES

9. Plaintiff Physicians Committee for Responsible Medicine ("PCRM") is a national nonprofit membership organization headquartered in Washington, DC. PCRM is committed to promoting a safe and healthful diet and to protecting consumers from food and drink that are dangerous or unhealthful. PCRM also advocates the use of scientific research methods that are both effective and ethical. In 2004, PCRM joined a Rulemaking Petition submitted to EPA seeking repeal of the DNT Guidelines in order to promote these goals and to protect its members from the risk of adverse health effects from excessive exposure to pesticides.

10. Many of PCRM's more than 100,000 members and supporters joined the organization in order to obtain adequate representation of their interest in a safe and healthful diet free from risks, including developmental risks to their children. Many members of PCRM are vegetarians, and their diet consists of plant-based foods that are treated with pesticides, such as fruits, grains, nuts, vegetables and legumes. Pregnant members and the young children of members who are

consuming foods with pesticide levels higher than the Tenfold Safety Factor set by the FQPA may have been, and continue to be, injured by these higher pesticide exposures and the associated risks of developmental impairment. PCRM's pregnant members and young children of members include individuals who are exposed on their farms, in their rural farming communities, by eating foods consumed in their schools, restaurants, and homes, through contact with local farms, soil and other materials that may be contaminated with pesticides.

11. PCRM has a broad interest in ensuring that the health of its members and their children are preserved by EPA's proper application of federal laws intended to protect their health. PCRM brings this action on behalf of its members, and to safeguard its own organizational interest in procuring the healthiest and safest possible diet in the United States. The interests of PCRM and its members in eating a healthy, safe diet are harmed by the defendant's failure to comply with the mandate of the FQPA and the APA. EPA's failure to repeal, and its continuing reliance on, the DNT Guidelines present numerous potential adverse impacts and risks on the health and safety of the food and beverages PCRM members and their children have consumed, are consuming, and will continue to consume in the future.

12. Plaintiff People for the Ethical Treatment of Animals ("PETA") is a national nonprofit membership organization headquartered in Norfolk, Virginia. PETA is committed to protecting animals from exploitation and suffering, and to promote a safe and healthful diet. PETA also advocates the use of scientific research methods that are both effective and ethical. In September 2004, PETA submitted a Rulemaking Petition to EPA seeking repeal of the DNT Guidelines in order to promote these goals.

13. Many of PETA's more than 850,000 members are vegetarians, and their entire diet consists of plants subjected to pesticide treatment, such as fruits, grains, nuts, vegetables and

legumes. Pregnant members and the young children of members who are consuming foods with pesticide levels higher than the Tenfold Safety Factor set by the FQPA may have been, and continue to be, injured by these higher pesticide exposures and the associated risks of developmental impairment. PETA's pregnant members and young children of members include those who are exposed on their farms or rural communities and those who are exposed to pesticides on their foods and in their schools and homes through contact with the outdoors, local farms, soil and other materials which may be contaminated with pesticides.

14. PETA brings this action on behalf of its members, and to safeguard its own organizational interest in procuring the healthiest and safest possible diet in the United States. The interests of PETA and its members in eating a healthy, safe diet are harmed by the defendant's failure to comply with the mandate of the FQPA and the APA. EPA's failure to repeal, and its continuing reliance on, the DNT Guidelines present numerous potential adverse impacts and risks on the health and safety of the food and drinks PETA members and their children have consumed, are consuming and will continue to consume in the future.

15. Plaintiff Trulie Ankerberg-Nobis, a resident of Takoma Park, Maryland, is a member of PCRM and a registered dietician. She is a vegetarian and an advocate for a safe and healthy diet, as well as for effective and ethical scientific research. She knows that many of the fruits and vegetables that she consumes may have been treated with pesticides that have undergone DNT testing and for which the Tenfold Safety Factor has been removed or greatly reduced. Ms. Ankerberg-Nobis is pregnant. Ms. Ankerberg-Nobis may have additional pregnancies and children in the future. After she gives birth, Ms. Ankerberg-Nobis intends to breast feed her child, as well as any additional children she may have in the future. Ms. Ankerberg-Nobis is concerned about the impact that pesticides may have had, and may continue to have, on her and

her fetus, on the breast milk she will feed her infants, and on her young children. Ms. Ankerberg-Nobis had many experiences that give rise to serious concerns about the environmental impact, including that of pesticides, upon the proper neurological development of a child. Ms. Ankerberg-Nobis had a brother with serious learning disabilities who died of a brain tumor at 14 years of age. The doctors were unsure as to the cause of the child's learning disabilities and tumor, but there were serious concerns in the community about an environmental cause, as there was an unusually high incidence of cancers and tumors in the area. Ms. Ankerberg-Nobis also had an uncle with learning disabilities, the cause of which was never determined, who grew up in an agricultural area. Ms. Ankerberg-Nobis fears that environmental toxins, including pesticides, could be the cause of these unexplained neurodevelopmental impairments.

16. Ms. Ankerberg-Nobis was born in Ord, Nebraska, a rural, farming community, and lived there for the first year-and-a-half of her life. She also lived in Gladstone, Michigan, a rural area with a logging industry, for ten years of her childhood, after which she moved to Rockford, Michigan, where there were a large number of orchards. As an adult, Ms. Ankerberg-Nobis lived in Dekalb, Illinois and Batavia, New York, both farming communities. Ms. Ankerberg-Nobis also made regular visits to her grandparents in a farming community in Illinois. As a child, she would play in the cornfields behind her grandparents' house. Ms. Ankerberg-Nobis is concerned about the exposure to pesticides that she and her unborn child have received and continue to receive from various sources.

17. In order to provide the healthiest possible environment for her fetus, Ms. Ankerberg-Nobis eats a healthful diet full of fruits and vegetables, exercises moderately, receives regular prenatal medical care, including daily prenatal vitamins, and avoids high risk behaviors such as drinking alcohol or smoking. Nevertheless, Ms. Ankerberg-Nobis believes that her fetus and any

future children may have been, and may continue to be, adversely affected by unnecessary exposure to potential risks of developmental impairment as a result of EPA's failure to apply the full Tenfold Safety Factor for pesticide exposure to children, and the Agency's continued reliance upon, and failure to repeal, the DNT Guidelines. Should the DNT Guidelines be repealed, Ms. Ankerberg-Nobis believes that the Congressionally mandated Tenfold Safety Factor would better protect her and her children from exposure to levels of pesticides that pose potential risks of developmental impairment.

18. Plaintiff Robin Hummel is a member and supporter of PETA and a resident of Norfolk, Virginia. Ms. Hummel, a former Air Force Captain, is a vegetarian and an advocate for a safe and healthful diet, as well as for effective and ethical scientific research. She knows that many of the fruits and vegetable that she consumes may have been treated with pesticides that have undergone DNT testing and for which the Tenfold Safety Factor has been removed or greatly reduced. Ms. Hummel is pregnant and the mother of a 20-month-old daughter. Ms. Hummel may have additional pregnancies and children in the future. Ms. Hummel provided breast milk for her daughter and intends to do the same for her unborn child and any future children. Ms. Hummel is very concerned about the impact that pesticides may have had, and may continue to have, on her and her fetus while she is pregnant, on the breast milk she has provided and will provide her infants, as well as on her present and future young children. Ms. Hummel has had many personal experiences that have made her justifiably concerned about the environmental impact, including that of pesticides, on the healthy development of a child. Ms. Hummel grew up on a farm in Ohio where pesticides were used on crops such as soybeans, corn, and wheat, and she takes her family back to the farm two or three times a year. Ms. Hummel is concerned about the exposure to pesticides that she and her children have received and continue

to receive at her family's working farm. Ms. Hummel's maternal uncle was born mentally retarded. Ms. Hummel taught at a middle school in South Carolina where she was exposed to many children with birth defects and handicaps. Ms. Hummel believes that pesticide exposure may have played a role in these developmental impairments.

19. In order to provide the healthiest environment for her fetus, Ms. Hummel is careful to eat a healthful diet full of fruits and vegetables, to exercise moderately, to receive regular prenatal medial care, including daily prenatal vitamins, and to avoid high risk behaviors such as drinking alcohol or smoking. Nevertheless, Ms. Hummel fears that her fetus and child may have been, and may continue to be, adversely affected by unnecessary exposure to potential risks of developmental impairment as a result of EPA's failure to apply the full Tenfold Safety Factor for pesticide exposure to children, and the Agency's continued reliance upon, and failure to repeal, the DNT Guidelines. Should the DNT Guidelines be repealed, Ms. Hummel believes that the Congressionally mandated Tenfold Safety Factor would better protect her and her children from exposure to levels of pesticides that pose potential risks of developmental impairment.

20. Plaintiff Jennifer Reilly, a resident of Takoma Park, Maryland, is a member of PCRM and a registered dietician. She is a vegetarian and an advocate for a safe and healthy diet, as well as for effective and compassionate scientific research. She knows that many of the fruits and vegetable that she consumes may have been treated with pesticides that have undergone DNT testing and for which the Tenfold Safety Factor has been removed or greatly reduced. Ms. Reilly is pregnant with a due date in October 2005. Ms. Reilly may have additional pregnancies and children in the future. After she gives birth, Ms. Reilly intends to breast feed her child, as well as any additional children she may have in the future. Ms. Reilly is very concerned about the impact that pesticides may have had, and may continue to have, on her and her fetus while she is

pregnant, on the breast milk she will feed her infants, as well as on her future young children. Ms. Reilly has had many experiences that give her concern about the environmental impact, including that of pesticides, upon the proper development of a child. Ms. Reilly had a sibling who was born with multiple, serious deformities and survived only a short time. The doctors at the time were unsure as to the cause of the child's deformities. Ms. Reilly's mother grew up on a farm in New York. Ms. Reilly also has a cousin born with Russell Silver Syndrome, which impaired his development in the womb, requiring his premature delivery and resulting in his unusually short physical size. The cause of this syndrome is not understood. Additionally, Ms. Reilly's neighbor in Takoma Park gave birth to a child with a chromosomal disorder and severe mental retardation. Ms. Reilly fears that environmental toxins, including pesticides, could be the cause of these unexplained developmental impairments. Ms. Reilly lived in a rural, farming area when she attended Pennsylvania State University and volunteered on farms as part of a class on sustainable agriculture. Ms. Reilly also makes yearly visits to her uncle's farm in New York and to various other farms for apple picking. Ms. Reilly is concerned about the exposure to pesticides that she, her unborn child and any future children have or will receive from various agricultural products and facilities.

21. In order to provide the healthiest possible environment for her fetus, Ms. Reilly eats a healthful diet full of fruits and vegetables, exercises moderately, receives regular prenatal medial care, including daily prenatal vitamins, and avoids high risk behaviors such as drinking alcohol or smoking. Nevertheless, Ms. Reilly believes that her unborn child and future children may have been, and may continue to be, adversely affected by unnecessary exposure to potential risks of developmental impairment as a result of EPA's failure to apply the full Tenfold Safety Factor for pesticide exposure to children, and the Agency's continued reliance upon, and failure to

repeal, the DNT Guidelines. Should the DNT Guidelines be repealed, Ms. Reilly believes that the Congressionally mandated Tenfold Safety Factor would better protect her and her children from exposure to levels of pesticides that pose potential risks of developmental impairment.

22. Defendant Stephen L. Johnson is the Administrator of EPA, nominated by President Bush and confirmed by the Senate in 2005, and is being sued in his official capacity. Administrator Johnson is the official ultimately responsible for all activities of the Agency. EPA is based in Washington, DC and is responsible for implementing the federal law in this area, including the tenfold safety factor in the FQPA.

FACTUAL ALLEGATIONS

STATUTORY FRAMEWORK

A. TSCA and FIFRA DNT Guidelines

23. Plaintiffs' petition requested the repeal of the two DNT Guidelines, each of which constitutes a rule as defined by the APA, 5 U.S.C. § 551(4). The DNT Guideline established pursuant to 40 C.F.R. § 799.9630 and related to the Toxic Substances Control Act shall be referred to as the TSCA DNT. The DNT Guideline adopted under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), identified as OPPTS 870.6300, shall be referred to as the FIFRA DNT. Plaintiffs petitioned for repeal of the TSCA and FIFRA DNT on the following grounds: i) that they produce data of unproven reliability and relevance to humans, and therefore constitute unsound science, and ii) that they were adopted without notice and comment rulemaking in violation of § 553(b) of the APA.

24. According to EPA's *OPPTS Harmonized Test Guidelines*, the DNT is designed:

> [T]o develop data on the potential functional and morphological hazards to the nervous system, which may arise in the offspring from exposure of the mother during pregnancy and lactation…. The test substance is administered to several

> groups of pregnant animals during gestation and early lactation, one dose level being used per group. Offspring are randomly selected from within litters for neurotoxicity evaluation. The evaluation includes observations to detect gross neurological and behavioral abnormalities, determination of motor activity, response to auditory startle, assessment of learning, neuropathological evaluation, and brain weights.

25. The extraordinary complexity of these highly subjective measures, together with their dubious reliability and relevance to human beings, has created a litany of problems in the conduct and interpretation of DNT studies. In the words of EPA's own retrospective analysis of DNT studies:

> [D]ata must be examined in light of the many confounding factors that may have contributed to the study results and conclusions. Some of these factors are common to many or all of the studies, such as the influence of dose selection on determination of the NOEL [no-observed-effect-level], inaccuracies or inconsistencies in the conversion of dietary or inhalation dose levels to mg/kg/day values, a lack of knowledge regarding actual exposure of the chemical to offspring in utero or via the milk (pharmacokinetic data), or differences in the endpoints examined for the various protocols (for example, the timing of measurements, variations in laboratory procedures, missing or inadequate assessments of any particular endpoint). Some factors are specific to a chemical or a particular study protocol. These might include utilization of knowledge on the chemical to aid in the selection of tests to assess learning and memory or of the most appropriate species for testing. It is also acknowledged that the conclusions of the studies, as well as the endpoints selected for risk assessment, are often issues of contention between the Agency and the regulated community. There are ongoing, unresolved controversies regarding some of the studies presented in this paper as well as some of the Agency decisions cited in this analysis.

(Makris S, Raffaele K, Sette W and Seed J. *A Retrospective Analysis of Twelve Developmental Neurotoxicity Studies Submitted to the USEPA Office of Prevention, Pesticides and Toxic Substances (OPPTS).* Washington, DC: EPA (1998))

26. EPA test guidelines for DNT studies have existed in various draft and final forms since the 1980s. A DNT protocol was developed in 1988 by what was then EPA's Office of Toxic Substances (now the Office of Pollution Prevention and Toxics) for the assessment of

specific solvent chemicals, and codified at 40 C.F.R. § 795.250 (53 Fed. Reg. 5947, Feb. 26, 1988).

27. In 1991, the Agency finalized another DNT Guideline, OPP 83-6 (*Pesticide Assessment Guidelines, Subdivision F—Hazard Evaluation: Human and Domestic Animals, Addendum 10*, EPA Report 540/09-91-123, March 1991). This protocol was revised in 1998 into its current incarnation, OPPTS 870.6300, but has not been published in the Code of Federal Regulations. The following year, EPA issued a data call-in (DCI) for organophosphate pesticides (OPs), which imposed several new requirements for DNT testing over and above those prescribed in published DNT Guidelines (Footnotes and Key Definitions for Guideline Requirements, DCI Number: GDCI-059201-NNNNN). Consequently, "anyone who plans to conduct a DNT study really must address the requirements instituted via the DCI notice for the OPs because that represents the new standard" (Sheets L. *Experience Conducting Developmental Neurotoxicity Studies*. Transcript from a presentation delivered to The Toxicology Forum – Summer Meeting 2003. Aspen, CO: Toxicology Forum (2003)).

28. In 2000, EPA published yet another DNT Guideline, 40 C.F.R. § 799.9630, as part of a Final Rule entitled "*Toxic Substances Control Act Test Guidelines,*" 40 C.F.R. § 799 *et seq.* According to EPA's *Federal Register* notice: "Establishment of these guidelines provides a series of standardized test procedures and is necessary to ensure enforceable test standards in test rules promulgated under section 4 of TSCA" (65 Fed. Reg. 78746, Dec. 15, 2000). The notice further stated that EPA "is publishing this action as a final rule **without prior opportunity for notice and comment** because the Agency believes that providing notice and an opportunity to comment is unnecessary." [Emphasis supplied.]

29. In 2001, EPA provided pesticide registrants with additional "*Guidance on Cholinesterase Measures in DNT and Related Studies*," which further modified and added to the requirements of the DNT Guidelines.

B. FQPA and the Tenfold Safety Factor

30. The FQPA amended the Federal Food, Drug, and Cosmetic Act at 21 U.S.C. § 346a, to require that:

> [A]n additional tenfold margin of safety for pesticide chemical residue and other sources of exposure should be applied for infants and children to take into account potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children.

31. 21 U.S.C. § 346a(b)(2)(ii) further states:

> [T]he Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such a margin will be safe for infants and children."

The Act then defines "safe" as "**reasonable certainty that no harm will result from aggregate exposure**." 21 U.S.C. § 346a(b)(2)(ii). [Emphasis supplied.]

C. Validation and Test Verification Requirements

32. The Data Quality Act (DQA), 44 U.S.C. § 3516, reflects Congress' requirement that, as a matter of good public policy, governmental agencies ensure the "quality, objectivity, utility, and integrity of information disseminated by the agency…." The DQA's "Objectivity Standard" (Office of Management and Budget. *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies*, 67 Fed. Reg. 8452, http://whitehouse.gov/omb//fedreg/reproducible2.pdf. Washington, DC (2002); EPA. *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency*, pp. 57. Washington, DC

(2002)), requires EPA and its federal counterparts to ensure that information it disseminates is "accurate, reliable, and unbiased."

33. Likewise, for "Influential Scientific Information," such as data from a regulatory toxicity study, EPA's Data Quality Guidelines require that the Agency "ensure reproducibility for disseminated original and supporting data according to commonly accepted scientific, financial, or statistical methods" (EPA, 2002).

34. Congress has specifically mandated through creation of the permanent Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), 42 U.S.C. § 285l *et seq.*, that:

> [E]ach federal agency . . . shall ensure that any new or revised acute or chronic toxicity test method, including animal test methods and alternatives, is determined to be valid for its proposed use prior to requiring, recommending, or encouraging the application of such test method.

42 U.S.C. § 285l-4(c).

35. "Validation" is defined by ICCVAM and its international counterparts as "the process by which the reliability and relevance of a procedure are established for a particular purpose" (*ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods – NIH Publication No: 03-4508*. Research Triangle Park, NC, USA: ICCVAM/ NICEATM. (2003)). EPA's own Scientific Advisory Panel (SAP) has likewise emphasized:

> [T]hat any new test guideline adopted by the Agency requires validation. This entails producing reproducible results among laboratories and selection of endpoints in test animals that are applicable to humans.

SAP. *A Set of Scientific Issues being Considered by the Agency in Connection with the Use of FQPA 10X Safety Factors to Address Special Sensitivity of Infants and Children to Pesticides – Final Report*. Washington, DC (March 1998).

D. APA: Notice and Comment Rulemaking

36. The APA, 5 U.S.C. § 553, requires that

> **(b)** General notice of proposed rule making shall be published in the Federal Register . . . The notice shall include--
>
> **(1)** a statement of the time, place, and nature of public rule making proceedings;
>
> **(2)** reference to the legal authority under which the rule is proposed; and
>
> **(3)** either the terms or substance of the proposed rule or a description of the subjects and issues involved.
>
> **(c)** After notice required by this section, the agency shall give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments with or without opportunity for oral presentation. After consideration of the relevant matter presented, the agency shall incorporate in the rules adopted a concise general statement of their basis and purpose.

DNT GUIDELINES

A. DNT Is a Non-Validated Test and Is Not Reliable

37. No DNT Guideline or protocol, past or present, has ever been properly validated to confirm its reliability and relevance to neurodevelopmental effects in humans.

38. ICCVAM (2003) defines reliability as "a measure of the degree to which a test method can be performed reproducibly within and among laboratories over time." Ideally, reliability is assessed by means of a prospective validation study, in which the same standardized test method is performed in multiple laboratories to test a pre-determined series of test chemicals. Alternatively, reliability can be evaluated retrospectively, where historical data generated using a standardized method are available for a group of chemicals; however, this approach has a number of limitations and is generally less favorable than a prospective study. In either case, calculations are made regarding a test's intra- and inter-laboratory reproducibility

and repeatability, and a conclusion is reached as to its overall reliability.

39. The DNT Guidelines have not been subject to a level of scrutiny even remotely approximating that of a prospective, inter-laboratory validation study. Moreover, existing data and published assertions by EPA personnel do not inspire confidence in the reliability of data from DNT studies. For example, a study of behavioral tests (which represent a core component of the DNT Guidelines), "found extreme variability in the results [of replicate neurobehavioral studies] obtained in different laboratories" (Claudio L, Kwa WC, Russell AL and Wallinga D. Testing methods for developmental neurotoxicity of environmental chemicals. *Toxicology and Applied Pharmacology* 164, 1-14 (2000)). In this study, three different laboratories conducted a battery of six neurobehavioral tests in inbred strains of adult mice. The results varied widely among the laboratories, in spite of rigorous controls of methodological variables, including test apparatus, testing protocols, animal husbandry, acclimation times, order of administration of tests, etc. The results demonstrated that confounding influences in the laboratory environment produced widely different neurobehavioral outcomes (Crabbe JC, Wahlesten D and Dudek BC. Genetics of mouse behavior: Interactions within laboratory environment. *Science* 284, 1670-1672 (1999)).

40. Variability among DNT studies may be even greater than in the above example, due to the high degree of "flexibility" EPA permits in the choice of behavioral tests for learning and memory, as well as in the selection of strains and species of animals used in DNT studies (Cooper Rees D, Francis EZ and Kimmel CA. Scientific and regulatory issues relevant to assessing risk for developmental neurotoxicity: An overview. *Neurotoxicology and Teratology* 12, 171-181 (1990)). In the words of one high-ranking EPA neurotoxicologist: "the outcome of a [DNT] study can depend on the inherent variability of a test measure" (Tilson HA. Neurotoxicity

risk assessment guidelines: Developmental neurotoxicology. *NeuroToxicology* 21, 189-194 (2000)). This was clearly demonstrated by a recent EPA retrospective analysis of "positive control" data in DNT studies (Crofton KM, Makris SL, Sette WF, Mendez E and Raffaele KC. A qualitative retrospective analysis of positive control data in developmental neurotoxicity studies. *Neurotoxicology and Teratology* 26, 345-352 (2004)). The authors note that: "[a] necessary property of a good positive control chemical is that the effects on the endpoint of concern are well-characterized and accepted by the general scientific community." Thus, positive controls in the context of DNT studies are substances that have been well established to be toxic to neurodevelopment. Significantly, however, EPA's retrospective analysis found that "[l]ack of effect of the positive control chemical was a problem that occurred at least once in over 50% of the [16] test laboratories" (Crofton et al., 2004). This suggests that DNT results often cannot even be duplicated from one laboratory to another.

B. Factors Showing Lack of Relevance to Humans of DNT Testing

41. The ultimate goal of DNT testing is to predict with confidence the neurotoxic potential (or lack thereof) of a test chemical in human infants and children by the extrapolation of data from laboratory experiments on animals. Thus, establishing the relevance of the DNT, or "the extent to which a test method correctly predicts or measures the biological effect of interest in humans or another species of interest" (ICCVAM, 2003), is of vital importance to demonstrating the relevance of the test. However, the relevance to humans of laboratory tests on rodents and other animals in general is the subject of much controversy, due to the myriad of biological differences that exist between animal species, as well as methodological issues such as chemical dosing, behavioral measures, etc. (Derelanko MJ and Hollinger MA (Eds.). *Handbook of Toxicology, Second Ed.*, pp. 1277-1280. Washington, DC: CRC Press (2002)).

42. One source of doubt regarding the relevance of animal-based test results to human hazard and risk assessment stems from the fact that different animal species—and even different strains within a species—can process chemicals quite differently. Inter-species differences can take many forms, including the rate and degree of chemical absorption, the manner in which it is circulated throughout the body and the organ(s) that may be targeted, the manner in which it is bio-transformed into active or inactive metabolites, and finally, the rate at which it is eliminated from the body (Stanton ME and Spear LP. Workshop on the qualitative and quantitative comparability of human and animal developmental neurotoxicity – Workgroup 1 report. *Neurotoxicology and Teratology* 12, 261-267 (1990)).

43. For example, as cited by Claudio and colleagues (2000):

> [T]halidomide has been shown to cause limb malformations in the human fetus when exposed just once to the chemical at doses of 0.5-1.0 mg/kg. Rats, when given doses as high as 3500 mg/kg, show no teratogenic effects [birth defects]…. Effects from exposure to organophosphate pesticides (OPs) also vary among different species. For example, delayed neurotoxicity is observed in OP-exposed humans and chickens, but may not be observed in primates, rats, and rabbits….

44. Another reason that DNT testing is not relevant for extrapolation to humans relates to strain sensitivity (that is how different genetic variants of an animal—e.g., mice—react differently to the same substance). An EPA-commissioned *White Paper on Species/Strain/Stock in Endocrine Disruptor Assays* (Parker SP and Tyl RW. Contract No. 68-W-01-023. Washington, DC: EPA (25 July 2003)), which compared the sensitivity of various rodent species and strains to selected chemicals across various toxicity endpoints, reported wildly conflicting findings. For example, one study examining the effects of the chemical ethinyl estradiol (EE) on uterine weight found Sprague-Dawley (SD) rats to be the most sensitive strain, while an almost identical study reported that SD rats were the least sensitive strain for the purpose of detecting

the effects of the same chemical on the same endpoint.

45. The magnitude and confounding effect of species differences in DNT studies were specifically addressed by an EPA Workshop on the Qualitative and Quantitative Comparability of Human and Animal Developmental Neurotoxicity. Based on an examination of no-observed-adverse-effect-levels (NOAEL) obtained in DNT studies conducted in a variety of species, the workshop acknowledged that there was "a wide range of differences across species (up to a 10,000-fold difference)" (Francis EZ, Kimmel CA and Rees DC. Workshop on the qualitative and quantitative comparability of human and animal developmental neurotoxicity: Summary and implications. *Neurotoxicology and Teratology* 12, 285-292 (1990)). This workshop further concluded that, "[i]n many cases—for example, lead, PCBs, and radiation—the proposed [DNT testing] battery probably would have underestimated human risk. This is true even when uncertainty factors are taken into account" (Stanton et al., 1990).

46. The relevance of DNT studies is also undermined by the differences in developmental-pattern-dependent exposure. In addition to species differences in toxicokinetics (i.e., route and rate of chemical absorption, metabolism, transport in the body, and elimination), the interpretation of DNT studies is confounded by the fact that animal species are born at developmentally different stages and mature at markedly different rates (Miller D. *Study Design and Critical Review of Functional and Morphological Endpoints.* Transcript from a presentation delivered to The Toxicology Forum – Summer Meeting 2003. Aspen, CO: Toxicology Forum (2003)). The NRC examined this issue in its 1993 report, *Pesticides in the Diets of Infants and Children*, noting:

> The newborn rabbit, rat, mouse and hamster can double their birth weights in less than one week, much faster than the human infant can. These different growth velocities may alter the toxicity of pesticides and other chemicals among different

> species of infant animals…. The age period in which specific organs or tissues undergo their most rapid rate of development and the age at which development is completed have major implications for studies of toxicity to those organs in growing animals…. Thus, the impact of toxic products can produce quite different outcomes that vary both with time and with species.

pp. 29-30.

47. Rats, the recommended species in the DNT Guidelines, differ from humans in a number of other important developmentally relevant ways. Dorman and colleagues (Dorman DC, Allen SL, Byczkowski JZ, Claudio L, Fisher JE Jr, Fisher JW, Harry GJ, Li AA, Makris SL, Padilla S, Sultatos LG and Mileson BE. Methods to identify and characterize developmental neurotoxicity for human health risk assessment: Pharmacokinetic and pharmacodynamic considerations. *Environmental Health Perspectives* 109 (Suppl. 1), 101-111 (2001)) have cautioned that:

> There are marked interspecies differences in types of placenta, orientation of exchanging vessels, and number of exchanging layers…. [L]arge species differences have been shown for placental permeability of hydrophilic molecules…. The observed species differences in placental transfer of hydrophilic xenobiotics are caused predominantly by structural differences among placenta.

Such differences may have a profound effect on the extent to which unborn rat and human fetuses are exposed to a chemical in the womb.

48. The relevance of DNT test results to humans is further diminished by the dosing methods of the test procedures. The DNT Guidelines specify that, "the test substance … should be administered orally," which can include the addition of a test substance to an animal's diet, drinking water, or pumping it directly into an animal's stomach (known as "gavage" administration). It is well established that chemical exposure via oral gavage has the potential to deliver chemicals to a target site at a rate that far exceeds anything that would occur in the real world (Conolly RB, Beck BD and Goodman JI. Forum: Stimulating research to improve the

scientific basis of risk assessment. *Toxicological Sciences* 49, 1-4 (1999)).

49. A further issue of concern with respect to the relevance and reliability of DNT results is EPA's specification that, "…the highest dose level should be chosen with the aim to induce some maternal toxicity (e.g., clinical signs, decreased body weight… and/or evidence of toxicity in a target organ)." Problems arise because, as EPA's Tilson (Tilson HA. Study design considerations in developmental neurotoxicology. *Neurotoxicology and Teratology* 14, 199-203 (1992)) acknowledges: "agent-induced maternal toxicity can contribute to behavioral indicators of neurotoxicity in the offspring, confounding interpretation of the data."

50. Factors such as impaired maternal care behavior (e.g., nurturing and grooming), while critical to the growth and development of offspring, are not assessed in the DNT Guidelines (Sheets L. *Experience Conducting Developmental Neurotoxicity Studies.* Transcript from a presentation delivered to The Toxicology Forum – Summer Meeting 2003. Aspen, CO: Toxicology Forum (2003)). Nutrition is likewise critical to pups' growth and development, yet milk quantity and quality are not evaluated, nor are measurements recorded of components in the milk (Sheets, 2003). Maternal toxicity during the *in utero* phase may be equally problematic, as a result of reduced maternal food consumption, maternal pulmonary damage, maternal renal damage, effects on the maternal central nervous system, etc. (Tyl RW and Sette WF. Workshop on the qualitative and quantitative comparability of human and animal developmental neurotoxicity – Workgroup III report: Weight of evidence and quantitative evaluation of developmental neurotoxicity data. *Neurotoxicology and Teratology* 12, 275-280 (1990)). Thus, "under circumstances of severe toxicity, you cannot distinguish whether effects are due to developmental neurotoxicity or secondary to maternal toxicity" (Sheets, 2003).

51. Another factor related to dosing that diminishes the relevance of DNT testing is the

inability to determine the amount of a chemical actually reaching a fetal or nursing pup. Because developing animals are exposed to a test substance via the dam—which relies on transport of the substance through the placenta or via lactation—the actual level(s) and route(s) of exposure in the pups are highly speculative (Claudio et al., 2000; Dorman et al., 2001).

> Behavioral testing has become a central component of DNT studies due to the perceived sensitivity of behavioral endpoints in detecting subtle chemical insults to the central nervous system. However, current measures of an animal's cognition, sensory-motor function, and other behavioral parameters are numerous and diverse, often differing widely in terms of the subjectivity of observations, breadth and specificity of results, quantity and quality of available validation data, and extrapolation of results among species

(Cory-Slechta DA, Crofton KM, Foran JA, Ross JF, Sheets LP, Weiss B and Mileson B. Methods to identify and characterize developmental neurotoxicity for human health risk assessment: Behavioral effects. *Environmental Health Perspectives* 109 (Suppl. 1), 79-91 (2001)).

52. As detailed by Anger (Anger WK. Worksite behavioral research: Results, sensitive methods, test batteries and the transition from laboratory data to human health. *NeuroToxicology* 11, 629-720 (1990)), laboratory tests employed to assess the effects of chemicals in animals "differ markedly" from those used to assess neurotoxic effects in humans. Anger's comparison of laboratory and human clinical and occupational assessment techniques "reveals a lack of parallelism between the screening tests that will be employed to test animals and those used to assess humans, suggesting that the respective tests do not test similar functions." For example, sensory tests in human volunteers include sophisticated measures of visual perception and memory, whereas the animal-based tests for sensory function include simplistic "finger snap response," "tail pinch response," and "pupil response" (Anger, 1990). Exacerbating this problem is the question of whether current behavioral measures of learning and memory can accurately be

applied early in a rodent's life span, and whether they are sufficiently sensitive to detect subtle effects on the central nervous system (SAP, 1999; Claudio et al., 2000). Indeed, the Agency's SAP "was divided whether the methods identified [in EPA's DNT guidelines] are reasonable for assessment of toxicity to offspring."

53. Also widely recognized is the fact that reliance on often-subjective behavioral observations, versus more objective physiological measures, has the potential to introduce major uncontrolled variability into conduct and interpretation of DNT studies (Claudio et al., 2000; Tilson HA. The concern for developmental neurotoxicology: Is it justified and what is being done about it? *Environmental Health Perspectives* 103 (Suppl. 6), 147-151 (1995); Gerber GJ and O'Shaughnessy DO. Comparison of the behavioral effects of neurotoxic and systemically toxic agents: How discriminatory are behavioral tests of neurotoxicity? *Neurobehavioral Toxicology and Teratology* 8, 703-710 (1986)). Studies that have relied upon neurobehavioural tests have suffered from poor inter-laboratory reproducibility, even where rigorous control has been maintained over variables such as test apparatus, testing protocols, animal husbandry, acclimation times, order of administration of tests, etc. (Crabbe JC, Wahlesten D and Dudek BC. Genetics of mouse behavior: Interactions within laboratory environment. *Science* 284, 1670-1672 (1999)). This situation is particularly worrisome in view of the fact that EPA's DNT Guidelines allow investigators considerable "flexibility" in their choice of methods of behavioral testing.

54. Another concern regarding the relevance of the DNT Guidelines to conclusions regarding humans relates to the specificity of behavioral tests for neurotoxicity, or their ability to distinguish between "true" neurotoxicity as distinct from more generalized systemic toxicity. This question was examined by Gerber and O'Shaughnessy (1986), who concluded:

> These results further illustrate the point that none of the standard behavioral tests are unique indicators of impaired central nervous system function. All the behavioral tests used in this study were affected by impairment of critical systemic organs as well as by restriction of food and water intake. Before it can be concluded that a compound is neurotoxic on the basis of behavioral test results, it must be ascertained that non-neural organs have not been damaged by the test compound, and that food and water consumption have not been severely decreased. Unless these factors are considered, it is possible to obtain a behavioral test result that suggests a neurotoxic effect, but which is actually the consequence of systemic organ toxicity.

55. In an attempt to overcome some of these well-known and serious limitations, EPA turned to the International Life Sciences Institute (ILSI) for assistance. ILSI's Risk Science Institute responded by convening a working group of experts from government, industry, academia and the public interest sector to review these issues (Mileson BE and Ferenc SA. Methods to identify and characterize developmental neurotoxicity for human health risk assessment: overview. *Environmental Health Perspectives* 109 (Suppl. 1), 77-78 (2001)). The report of the ILSI working group on behavioral effects was particularly enlightening, noting, among other things, that "…there are numerous examples of the misuse of these methods and misinterpretation of results derived from these methods" (Cory-Slechta DA, Crofton KM, Foran JA, Ross JF, Sheets LP, Weiss B and Mileson B. Methods to identify and characterize developmental neurotoxicity for human health risk assessment: Behavioral effects. *Environmental Health Perspectives* 109 (Suppl. 1), 79-91 (2001)).

56. Another factor that reveals the unreliability of the DNT Guidelines is the:

> [L]imited understanding of the morphological basis of developmental neurobehavioral disorders. Our ignorance is exemplified at one extreme by debilitating disorders that do not appear to be associated with any detectable morphologic defect. At another extreme is the occurrence of dramatic congenital alterations in the brains of individuals that exhibit only minimal, if any, functional impairments."

(Jensen KF and Catalano SM. Brain Morphogenesis and Developmental Neurotoxicology, pp. 3-

14. In: *Handbook of Developmental Neurotoxicology* (Eds: W Slikker Jr & LW Chang). Academic Press (1998)). It should therefore come as no surprise that the ILSI working group on neuropathology assessment (Garman RH, Fix AS, Jortner BS, Jensen KF, Hardisty JF, Claudio L and Ferenc S. Methods to identify and characterize developmental neurotoxicity for human health risk assessment: Neuropathology. *Environmental Health Perspectives* 109 (Suppl. 1), 93-100 (2001)) identified a litany of potential confounding factors and other limitations associated with DNT studies.

57. Among the conclusions of the ILSI neuropathology working group was that:

> Differences between species in the rates and complexities of biologic processes underlying neurologic development contribute significantly to the challenge of using animal species, such as the rat, to predict the neurotoxic potential of a chemical in humans.

(Garman et al., 2001).

58. In the absence of proper validation, EPA cannot conclude that the results of DNT studies have any bearing on the potential threat of the investigated substance to humans—much less our children. This conclusion was expressed by a panel of the National Academy of Sciences, which reported: "the subcommittee finds that the developmental neurotoxicity test, as it is currently described in the U.S. Environmental Protection Agency (EPA) guidelines (EPA 1991), might be inadequate to identify and characterize specific developmental neurotoxicants (Commission on Life Sciences. *Methyl Bromide Risk Characterization in California*, p. 60. Washington, DC: National Academy Press (2000)).

59. In the words of one EPA scientist:

> It is clear from comparison of the human and rodent data that the results from rodent studies often vastly underestimate intakes at which neurotoxicity was observed in humans. For lead, deficits were revealed on activity and simple learning tests at doses that would also result in allowable intakes much higher

> than those at which cognitive impairment has been demonstrated for children. One conclusion that may be drawn from this analysis is that current methods of calculating acceptable intakes based on animal data … are insufficient to protect the human population against behavioral toxicity.

(Rice DC, Evangelista de Duffard AM, Duffard R, Iregnen A and Satoh H. Lessons for neurotoxicity from selected model compounds. *Environmental Health Perspectives* 104 (Suppl. 12) 205-215 (1996)).

60. Likewise, when asked by the Agency for its opinion as to the sensitivity of the DNT relative to other developmental and reproductive toxicity studies, EPA's SAP stated: "The DNT is not more sensitive in its current form, given what is known in the broader neuroscience and pediatric community…. Therefore, the current form of the DNT guidelines … is not a sensitive indicator of toxicity to the offspring" (SAP, 1999).

C. Test Method Evaluations by ICCVAM

61. ICCVAM validation criteria (2003) reflect not only the perspectives of 15 federal agencies in the U.S., but the consensus reached by regulatory community globally, under the auspices of the 30-member-country Organization for Economic Cooperation and Development (OECD. *Final Report of the OECD Workshop on Harmonization of Validation and Acceptance Criteria for Alternative Toxicological Test Methods*, 49 pp. Paris, France: OECD (1996)). Since its inception, ICCVAM has evaluated the scientific validity (i.e., reliability and relevance) of more than a dozen new and revised toxicity test methods relative to its internationally accepted criteria. In so doing, ICCVAM and scientific peer review panels it has convened have issued recommendations in support of—or in opposition to—regulatory applicability and acceptance of specific test methods. Significantly, when ICCVAM was asked to validate a test with dubious reliability and relevance similar to that of DNT—e.g., FETAX (ICCVAM. *FETAX – Frog*

Embryo Teratogenesis Assay-Xenopus – Background Review Document, Website http://iccvam.niehs.nih.gov/methods/fetaxdoc/fetaxbrd.htm. Research Triangle Park, NC, USA: ICCVAM/NICEATM (2000))—the method was summarily rejected on the grounds that it "…is not sufficiently validated or optimized to be used for regulatory applications" (ICCVAM. *Expert Panel Meeting on the Frog Embryo Teratogenesis Assay-Xenopus (FETAX): A Proposed Screening Method for Identifying Developmental Toxicity Potential of Chemicals and Environmental Samples*. Website http://iccvam.niehs.nih.gov/docs/ minutes/fetaxMin.pdf. Durham, NC, USA, May 16-18, 2000). In light of the numerous documented limitations of the DNT Guidelines, there can be little doubt that they too would face invalidation and rejection by ICCVAM, which may explain why such an evaluation has never taken place.

D. Public Policy Considerations

62. There are several public policy considerations expressed in the ICCVAM Authorization Act, the National Institutes of Health Revitalization Act of 1993 (42 U.S.C. § 283e), the FQPA, and the DQA that positively support the merits of this case. These Acts express, respectively, Congressional intent that toxicity test methods be validated, as well as the reduction, refinement, and ultimate replacement of animal use in toxicity testing, the precautionary regulation of pesticides and other chemicals, and the soundness and integrity of information disseminated and used by federal agencies. Each Act highlights the arbitrariness of EPA's action in denying Plaintiffs' petition and continuing to implement the DNT Guidelines.

63. One of the central aims of the ICCVAM Authorization Act is to promote and advance alternatives to animal-based testing. In establishing the 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. At least 1,300 animals are killed for every DNT Guideline study that is performed—although for practical purposes, "anyone who plans to conduct a DNT study really must address the requirements instituted via the DCI notice for OP's because that represents the new standard" (Sheets, 2003). This revised study design may kill as many as 2,600 animals (Mattsson JL, Eisenbrandt DL and Doe JE. *More Than 10,000 Animals Are Required for the Registration of a Single Pesticide – This Paradigm Must Be Changed*. Poster Presented at 2003 Meeting of the Society of Toxicology) at a cost of up to $1 million per active ingredient (Werner KL. *Companies Question Agency's Changes for Developmental Neurotoxicity Study*. 24 BNA 535 (March 20, 2000)). Moreover, to the extent the DNT has been revised, it was done so without being validated as called for in the statute.

64. The NIH Revitalization Act of 1993 directs the National Institutes of Health, through an Interagency Coordinating Committee on the Use of Animals in Research, to prepare a plan 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. It is clear from the language of the statute that Congress intended for EPA to be an active contributor to development and implementation of the above-mentioned plan, as involvement by "representatives of the Environmental Protection Agency…" on the interagency committee is a specific requirement under the Act.

65. The FQPA and the DQA, discussed above, respectively promote application of the precautionary principle and the quality, objectivity, utility, and integrity of information

disseminated by the agency. The DNT Guidelines stand in stark contrast to the letter and spirit of both Acts.

66. From a public and children's health perspective, it is clear that given the uncertainties and subjectivity associated with the DNT, this test cannot provide "reasonable certainty" that infants and children are safe and adequately protected from adverse effects associated with pesticide or other chemical exposures. In fact, as evidenced by EPA's own retrospective analysis (Makris et al., 1998): the DNT generally does not detect effects at lower doses than existing toxicity studies, meaning that DNT results seldom drive EPA pesticide risk assessments, and did not cause a single chemical of the 12 in EPA's retrospective analysis to be regulated more stringently (i.e., lowering of pre-existing reference doses).

67. The results of the FIFRA and TSCA DNT Guidelines and other similarly non-validated animal tests have been used over and over again by EPA to override the Tenfold Safety Factor mandated by the FQPA and thereby increase the level of certain pesticides to which infants and children are exposed. Thus, the repeal of the DNT Guidelines would protect children from unnecessarily high levels of pesticide exposure, otherwise allowed by reliance upon a highly questionable testing methodology that needlessly kills tens of thousands of animals without producing data relevant to potential developmental neurotoxicity in humans.

68. EPA has consistently taken the position that the DNT Guidelines and the data derived from their application are critical to any decision to allow a deviation from the Tenfold Safety Factor. EPA's pattern and practice is that, as to any given chemical, unless the DNT Guidelines are employed, a "data gap" exists and the Agency requires application of the Tenfold Safety Factor (HIARC/FQPA SFC, 1998). If the DNT Guidelines are repealed, EPA will adhere to the FQPA.

E. EPA Did Not Provide for Notice and Comment of DNT Guidelines

69. Notice of availability of the FIFRA DNT and approximately 60 other draft OPPTS test guidelines was published in the *Federal Register* on June 20, 1996, and interested persons were invited to submit written comments. 61 Fed. Reg. 31522. More than two years later, on August 5, 1998, EPA published notice of availability of final test guidelines, which included the FIFRA DNT. 63 Fed. Reg. 41845. However, this guideline was never promulgated as a Final Rule or published in the Code of Federal Regulations.

70. EPA has on multiple occasions required pesticide registrants to conduct DNT studies, both through a 1999 data call-in ("DCI") initiative and as a condition of registration under FIFRA § 3(c)(7)(B) and § 3(c)(7)(C).

71. EPA's 1999 DCI notice for organophosphate pesticides (OPs) imposed several new requirements over and above those required pursuant to FIFRA DNT. Consequently, "anyone who plans to conduct a DNT study really must address the requirements instituted via the DCI notice for the OPs because that represents the new standard" (Sheets, 2003).

72. Subsequent to the 1999 DCI, EPA provided pesticide registrants in October 2001 with supplemental "*Guidance on Cholinesterase Measures in DNT and Related Studies*" (EPA, 2001), which further modifies and adds to the requirements of the FIFRA DNT.

73. None of these modifications and additional requirements for DNT testing and creation of DNT Guidelines were adopted and instituted pursuant to APA notice and comment procedures.

F. EPA's Jan. 3, 2005 Denial of Plaintiffs' Rulemaking Petition

74. On January 3, 2005, the Acting Assistant Administrator of EPA's Office of Prevention, Pesticides and Toxic Substances, Susan B. Hazen, on behalf of the Agency, formally responded to PETA's and PCRM's Rulemaking Petition seeking repeal of the DNT Guidelines.

75. Although EPA acknowledged that there are weaknesses in the testing performed pursuant to the DNT Guidelines, the Agency hides behind the claim that the existing DNT protocol represents the "best available science" at this time. (EPA Response at 10). Whatever can be said about quality and reliability of the so-call "science" behind the DNT, it does not alter the fact that the DNT Guidelines **are not good enough**. As a matter of law, the FQPA at 21 U.S.C. § 346a(b)(2)(C), requires that:

> [A]n additional tenfold margin of safety for pesticide chemical residue and other sources of exposure should be applied for infants and children to take into account potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children.

While the Administrator may use a lower margin of safety, he may do so only; 1) on the basis of **reliable data, and**, 2) if he finds such a margin will be safe for infants and children. Critically, the statute defines "safe" at 346a(b)(2)(ii):

> [T]he term "safe," . . . means the Administrator has determined that there is a **reasonable certainty that no harm will result** from aggregate exposure. [Emphasis supplied.]

76. This provision of the statute creates a critical difference between this case and virtually every other challenge to scientific judgments made by EPA. Ordinarily, given the arbitrary and capricious standard set by the APA, EPA's decisions will be upheld so long as it can make the slight showing that there is some colorable scientific support for the decision it takes. The FQPA significantly limits the discretion of the Administrator, for he may not deviate from the Tenfold Safety Factor in the absence of **reasonable certainty**. While the FQPA does

not define that term, the word "certain" is defined in *Webster's Unabridged Dictionary* (2nd Ed. 2001) as "free from doubt or reservation." Whatever EPA can say in defense of the DNT Guidelines, the results of such tests are not "free from doubt." Thus, EPA's use and reliance on the DNT Guidelines to permit deviations from the Tenfold Safety Factor is arbitrary and capricious and in violation of law. EPA has allowed itself to be swayed by pressures from various interest groups into reaching a different, arbitrary, and unlawful conclusion.

77. In response to the allegations in Plaintiffs' Petition that EPA failed to promulgate the FIFRA DNT as a rule and to give public notice and an opportunity for public comment with respect to the TSCA DNT, the Agency stated that the FIFRA DNT is intended to be non-binding and that the Guideline will be reviewed in order to assure that this intent is adequately communicated. EPA further responded that while the TSCA DNT is written in with mandatory language, this does not make it mandatory and that, in any event, public notice and comment was not required because it was "unnecessary." (EPA Response at 14-16). EPA may not deviate from the APA by claiming that the DNT Guidelines are not rules, when the Agency makes use of them mandatory.

PLAINTIFFS' CAUSES OF ACTION

COUNT I

(Denial of Rulemaking Petition as Violation of the APA)

78. Plaintiffs repeat and reallege the prior allegations of the complaint.

79. EPA's denial of Plaintiff's Rulemaking Petition was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" in violation of the APA. 5 U.S.C. § 706(2)(a). First, it is arbitrary and capricious to mandate the use of the DNT Guidelines when they have not been validated and the results are not relevant or reliable. Second, and more

critically, it is arbitrary and capricious to use the data generated by tests under the DNT Guidelines to permit exposures of children to chemicals in amount which are not safe, in violation of the FQPA. EPA's violation of the APA has injured the plaintiffs and will continue to injure the plaintiffs by exposing PCRM's and PETA's members, and the individual plaintiffs and their unborn, current, and future children, to unnecessarily high levels of pesticides.

COUNT II

(Violations of Notice and Comment Rulemaking under The APA)

80. Plaintiffs repeat and reallege the prior allegations of the complaint.

81. EPA violated the APA by failing to promulgate the FIFRA DNT as a rule and by promulgating the TSCA DNT as a final rule without public notice and an opportunity for public comment. The Agency's circumvention of formal rulemaking procedures (i.e., through the amendment of its pesticide registration data requirements as codified under 40 C.F.R. § 158.340 and § 158.490) represents a violation of the APA's notice and comment rulemaking requirements. The Agency has systematically used DCIs, "guidelines" and "guidance documents" as a means to avoid notice and comment rulemaking in a manner that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" in violation of the APA. 5 U.S.C. § 706(2)(a).

82. EPA's violation of the APA has injured the plaintiffs and will continue to injure the plaintiffs by preventing them from having their voices heard and participating in the notice and comment rulemaking process required by the APA. Plaintiffs are further injured in that the results of EPA "closed door" decision-making, in violation of APA, has the effect of exposing PCRM's and PETA's members, and the individual plaintiffs and their unborn, current, and future children, to excessive levels of pesticides.

PRAYER FOR RELIEF

WHEREFORE, plaintiffs respectfully request that this Court enter judgment in their favor and against EPA and its Administrator:

(1) Declaring that by denying PCRM's and PETA's Rulemaking Petition seeking repeal of the DNT Guidelines, EPA has violated the APA; and

(2) Declaring that by issuing the FIFRA and TSCA DNT Guidelines without allowing for proper public notice and comment, EPA has violated the APA; and

(3) Setting aside, reversing and remanding EPA's January 3, 2005 Response denying PCRM's and PETA's Rulemaking Petition and Order that the Agency render a new decision on the Petition, consistent with this Court's Opinion, within sixty days; and

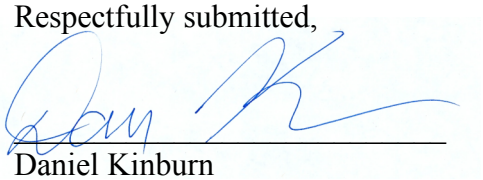
(4) Retaining jurisdiction of this matter until defendant has fulfilled all of its statutory, regulatory, and Court-Ordered obligations; and

(5) Awarding plaintiffs their costs, attorneys' fees, and other disbursements for this action, including any expert witness fees; and

(6) Granting plaintiffs such other and further relief as this Court may deem just and proper.

DATED: JULY 11, 2005

Respectfully submitted,



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