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Via mail and fax: 212.727.1773

Ms. Frances Beinecke
Executive Director
Natural Resources Defense Council
40 West 20th St.
New York, NY 10011

Dear Ms. Beinecke:

I am in receipt of your April 1, 2004 letter to PETA member , and would like to take this opportunity to address some of the points that you raise.

To begin, your comments seem to suggest that the Natural Resources Defense Council (NRDC) believes that in order to be considered scientifically valid, a non-animal test method must first undergo a validation review by the U.S. Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). This would seem to be the NRDC's position even in the case of test methods that have undergone rigorous validation and/or achieved regulatory acceptance in other countries. For example, the 3T3 Neutral Red Uptake (NRU) Phototoxicity Test and human skin equivalent tests for dermal corrosivity (e.g., EpiDerm™) have undergone successful validation through the European Centre for the Validation of Alternative Methods (ECVAM), and have been accepted by European regulators pursuant to an amendment of Annex V of EU Directive 67/548,[1] as well as by member countries of the Organization for Economic Cooperation and Development (OECD) in the form of OECD Test Guidelines 431[2] and 432,[3] respectively.

With respect to skin corrosivity, you note that ICCVAM has recommended that EpiDerm™-like human skin equivalent tests be used only as "positive screens," whereby negative results *in vitro* would trigger "confirmatory" animal testing.[4] Setting aside the obvious absurdity of relying on a non-validated animal test to "confirm" the results of a validated non-animal test, it is important to recognize that ICCVAM's position is not consistent with an otherwise international scientific and regulatory consensus on this matter. As noted above, all 30 OECD member countries (including the U.S.) agreed that the use of animals in skin corrosivity testing can be *totally eliminated* by means a non-animal weight-of-evidence determination combining pH measures, computerized structure-activity relationship (SAR) modeling, and a human skin equivalent assay such as EpiDerm™. OECD Test Guideline 431 specifically "allows for the identification of *non-corrosive* substances and mixtures when supported by a weight of evidence determination *using non-animal methods*"[2] (*my emphasis*).

Not only do ICCVAM's testing recommendations conflict with the scientific and regulatory conclusions reached by EU and OECD member countries, ICCVAM's position also appears to disregard the U.S.' obligations pursuant to the OECD's

[1] See "Validated Methods" section of http://ecvam.jrc.it
[2] OECD Test Guideline 431: http://www.oecd.org/dataoecd/56/45/28301734.pdf
[3] OECD Test Guideline 432: http://www.oecd.org/dataoecd/32/53/2077705.pdf
[4] http://iccvam.niehs.nih.gov/methods/epiddocs/cwgfinal/cwgfinal.htm

policy on Mutual Acceptance of Data. This OECD Council directive provides that "data generated in a Member country in accordance with OECD Test Guidelines and Principles of Good Laboratory Practice (GLP) shall be accepted in other Member countries for assessment purposes and other uses relating to the protection of human health and the environment."[5] Thus, refusal by a U.S. agency to accept *in vitro* skin corrosivity data generated in accordance with OECD Test Guideline 431 as stand-alone evidence of non-corrosivity would appear to constitute a breach of the U.S.' commitments vis-à-vis OECD Mutual Acceptance of Data.

The same would hold true for *in vitro* skin absorption data generated in accordance with OECD Test Guideline 428[6] and *in vitro* phototoxicity data generated using the validated 3T3 NRU Phototoxicity Test, as codified under OECD Test Guideline 432. U.S. agencies and other members of the OECD are not at liberty to reject or disregard *in vitro* data that have been generated in accordance with an internationally accepted OECD Test Guideline. As such, **is it truly the NRDC's position that even after 30 world governments have reached consensus as to the scientific validity and regulatory value of a non-animal test, the method must <u>still</u> be submitted to ICCVAM for additional evaluation before it can be considered valid and acceptable for use in the U.S.?** If so, why does the NRDC not insist upon ICCVAM review for all new and revised animal-based test methods (e.g., developmental neurotoxicity studies, which have never undergone formal scientific validation or evaluation by ICCVAM)?

On that note, I would also like to call your attention to a set of comments the NRDC filed in January 2004 with the U.S. National Toxicology Program (NTP). A recurring theme in the NRDC's comments was the "NTP rodent bioassay"—a $2 million study in which groups of at least 400 rats and 400 mice are dosed with a test chemical for their entire lifespan to see if they develop cancer. It is striking to note that even though the NRDC says that it supports the "appropriate integration of data from ... *in vitro* toxicity test methods," the NRDC "*strongly objects ... if a goal is to develop an alternative approach to the rodent bioassay*" (*my emphasis*). The NRDC goes on to suggest that its support for *in vitro* methods is tied primarily to their use in "trans-species extrapolations of toxic or carcinogenic effects." In other words, the NRDC appears to support *in vitro* methods only as a means of better interpreting the results of animal tests. The NRDC then goes on to criticize evidence from human population studies, while explicitly calling for more chemicals to be tested on animals in the NTP bioassay, i.e., "We encourage the NTP to *expand* this trusted methodology, to handle an *increased number of chemicals annually*" (*my emphasis*).

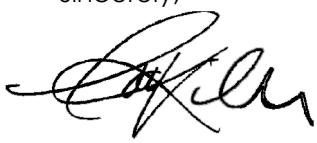
So on the one hand, you assure members of the public that the "NRDC strongly supports the adoption of modern technologies for chemical testing, and supports efforts to replace animal tests with validated non-animal alternatives where appropriate," while on the other, your staff "strongly object" to efforts to develop alternatives to animal tests, and actually go so far as to call for an increase in the amount of animal testing that is carried out! At the same time, your organization maintains a hypocritical double standard by advocating for non-validated animal tests such as developmental neurotoxicity and rodent cancer studies, while refusing to accept non-animal methods that have undergone rigorous and successful validation and/or have already been accepted by the regulatory community at the OECD level.

PETA has long held out the hope that we could find some common ground with the NRDC and engage in constructive advocacy on these issues. However, as should be clear from the examples I have cited, the positions being advocated by your staff on behalf of the NRDC have been so incredibly hostile toward non-animal test methods—as well as *any* effort to move away

[5] http://www.oecd.org/document/27/0,2340,en_2649_34365_1859419_1_1_1_1,00.html
[6] OECD Test Guideline 428: http://www.oecd.org/dataoecd/56/40/1946029.pdf

from animal testing—as to foreclose on any opportunities that might have existed. This is disappointing to say the least, as I feel that everyone—especially the creatures our organizations claim to represent—deserve better.

Sincerely,



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