August 16, 2006

Dr. William Stokes
Director of NICEATM
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Research Triangle Park, NC 27709

Via Electronic Mail to: stokes@niehs.nih.gov

Dear Dr. Stokes:

On behalf of the animal protection community, including the Doris Day Animal League, People for the Ethical Treatment of Animals, and the Physicians Committee for Responsible Medicine, we are submitting the following comments to the continuing SACATM dialogue regarding the "Peer Review Panel Report: The Use of *In Vitro* Basal Cytotoxicity Test Methods for Estimating Staring Doses for Acute Oral Systemic Toxicity Testing". Post the recent teleconference of the SACATM, which did not have a quorum, we respectfully request these comments be electronically forwarded to all members of the SACATM.

Having decades of experience advocating for good scientific advances in the field of *in vitro* methods, we are well aware of the pace of scientific successes. However, it continues to be a genuine concern that despite near unanimous agreement at the 2000 workshop that the cell-based methods could be used immediately to reduce the numbers of animals killed by setting the starting dose and that, within a few years – given the proper funding and effort – the method could be validated as a replacement measure, There has been no measurable progress on this critical issue.

ICCVAM has also issued a "Guidance Document on Using *In Vitro* Data to Estimate *In Vivo* Starting Doses for Acute Toxicity."1 To further the goal of validating the cytotoxicity tests as eventual replacement methods, EPA was prevailed upon to issue guidance to the participants of the HPV program. This guidance asked that sponsors use the in vitro method to set the starting dose if acute toxicity tests were to be conducted under the program: "The October 2000 Workshop concluded that in vitro cytotoxicity data could be useful in estimating starting doses for in vivo acute toxicity testing, and in this way could also reduce the number of animals used in subsequent in vivo tests." 2

1 NIH Pub. No. 01-4500
2 http://www.epa.gov/oppt/chemrtk/toxprtow.htm

A proposal was made at the SACATM meeting to focus on a possible first target for replacement of the animal test with an *in vitro* method(s), namely that the cytotoxicity methods could be used for testing those substances that are already known or suspected to be at the extremes of toxicity, and if the *in vitro* predictions corroborate the expectations from preliminary evidence, then no additional animal testing should be conducted for those substances. Several participants on the SACATM teleconference call commented on the strong correlation between the *in vitro* and *in vivo* data at the high dose/low toxicity end of the toxicity spectrum. This correlation supports the proposal and could lead to an immediate reduction in the number of animals used.

In addition, while the Report does not require the use of the *in vitro* methods to estimate a starting dose, due to the understandable contention that significant information may already be available on the chemical or its class, it is imperative that companies be encouraged to use the non-animal methods to obtain another level of comfort using and reading data generated by them.

We sincerely believe that the SACATM should, based on the available scientific evidence, at the very least recommend that the Report address expedient steps to replace lethal dose animal tests at the extremes of toxicity.

Sincerely,
Sara J. Amundson
Deputy Director
Doris Day Animal League

On behalf of : People for the Ethical Treatment of Animals
Physicians Committee for Responsible Medicine

cc: Ms. Jessica Sandler, PETA
Ms. Kristie Stoick, PCRM