

June 4, 2007

Dr Mary S. Wolfe  
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Re: **72 FR 23831; May 1, 2007; Public Comments Concerning the Draft  
NICEATM-ICCVAM 5-Year Plan (2008-2012)**

Dear Dr Wolfe:

People for the Ethical Treatment of Animals (PETA) is the world's largest animal rights organization, with 1.7 million members and supporters. We appreciate the continued opportunity to comment regarding the formulation of the draft NICEATM/ICCVAM 5-Year Plan (hereafter referred to as the "Draft Plan") by presenting oral comments at the meeting of SACATM June 12, 2007. Many of these comments reiterate those submitted by the animal protection community directly to NICEATM/ICCVAM.

Upon its inception in 1997, the animal protection community had great hopes for ICCVAM, whose intended purpose was to develop and promote regulatory acceptance of alternative methods that would refine, reduce and replace animal use in regulatory testing. However, in contrast to the intended purpose, ICCVAM has become, over the past decade, a major obstacle to the development and use of alternative, non-animal methods. In spite of progress in other countries, ICCVAM has repeatedly wasted its limited resources on duplicative studies that have hindered progress in the US.

For example, ICCVAM's few evaluations of the methods that have been validated in Europe by ECVAM and that have received endorsement by ICCVAM's European counterpart—the ECVAM Scientific Advisory Committee (ESAC), have resulted in either a restriction of use or a rejection of the method:

- ICCVAM and its US agency members continue to require that chemicals testing negative for skin corrosion (i.e., non-corrosive) *in vitro* be subject to "confirmatory" animal testing. Thus, while the EU and other OECD member countries have moved towards 100% replacement of animal use for skin corrosion testing<sup>1</sup>, ICCVAM's position allows for only a modest reduction in animal use.
- Nearly a year after ESAC endorsed the validity of five *in vitro* human blood-based tests for pyrogenicity<sup>2</sup>, ICCVAM undertook a second, full peer review of these methods. The ICCVAM-selected Peer Review Panel found fault with the new background documents ICCVAM had prepared and failed to recommend even the minimal use of these methods originally proposed by



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<sup>1</sup> <http://caliban.sourceoecd.org/vl=3371732/cl=15/nw=1/rpsv/ij/oecdjournals/1607310x/v1n4/s30/p1>

<sup>2</sup> [http://ecvam.jrc.it/publication/ESAC24\\_statement\\_pyrogenicity\\_1.pdf](http://ecvam.jrc.it/publication/ESAC24_statement_pyrogenicity_1.pdf)

ICCVAM, additionally recommending extensive parallel *in vivo/in vitro* validation studies.

- ESAC recently endorsed two *in vitro* methods for eye corrosion/severe irritation. ICCVAM reviewed these same methods in 2005 and published the Final peer review report in Nov. 2006; however, ICCVAM recommendations have yet to be transmitted to federal agencies
- ESAC has endorsed the conclusion that “the *in vitro* micronucleus test (MNT) is a scientifically valid alternative to the *in vitro* chromosome aberration (CA) assay for genotoxicity testing.”<sup>3</sup> This endorsement led to almost immediate regulatory acceptance of the MNT under the EU REACH chemicals regulation,<sup>4</sup> However, ICCVAM’s comments<sup>5</sup> regarding the draft OECD MNT Test Guideline did *not* reflect support for ESAC’s position, calling instead for substantial additional work before the MNT is accepted at the OECD level.
- Most recently, following ESAC endorsement of the validity of a variant of the Local Lymph Node Assay (rLLNA), under which animal use can be reduced by as much as 50%,<sup>6</sup> ICCVAM’s response was again been to propose a second peer review.

In addition, there are over a dozen alternative methods that have received ESAC endorsement that have yet to even be considered by ICCVAM.

ICCVAM has also demonstrated a lack of initiative in identifying and promoting alternative methods. In contrast to the dozens of methods being reviewed by its European counterpart, ICCVAM has promoted only three methods for international consideration, the Local Lymph Node Assay in 1999 (which uses fewer numbers of mice rather than guinea-pigs to test for skin allergy), the CORROSTEX<sup>®</sup> *in vitro* method for skin corrosion in 2000 (in contrast, ECVAM validated 3 other *in vitro* methods for skin corrosion), and the Up/Down method for estimating acute oral toxicity in 2000 (which reduces the number of rodents used; this method had been in place as an OECD guideline since 1998).

Another disappointment is ICCVAM’s failure to capitalize on its stated commitment to pursue *in vitro* methods of estimating acute oral toxicity. Following pressure from the animal protection community and the White House, ICCVAM convened an international workshop in 2000 to evaluate *In Vitro* Methods for Assessing Acute Systemic Toxicity. The result of this workshop was that ICCVAM recommended further evaluation of the use of *in vitro* cytotoxicity data as one of the approaches that could be used to *estimate the starting doses* (emphasis added) for rodent acute oral toxicity studies, and a Guidance Document was issued<sup>7</sup>. However, in the report from the 2000 workshop, the use of *in vitro* methods for estimating starting doses was to be considered an interim measure to immediately decrease the number of animals used; the report also states that “It was considered that, if the commitment to conducting a formal validation study was strong enough, the scientific resources could be harnessed for this effort with facility and the *in vitro* tests studied proved good enough, a replacement test battery might be achieved in as short a time as 2-3 years.”<sup>8</sup>

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<sup>3</sup> [http://ecvam.jrc.it/publication/ESAC25\\_statement\\_MNT\\_20061128.pdf](http://ecvam.jrc.it/publication/ESAC25_statement_MNT_20061128.pdf)

<sup>4</sup> [http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l\\_396/l\\_39620061230en00010849.pdf](http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_396/l_39620061230en00010849.pdf)

<sup>5</sup> <http://iccvam.niehs.nih.gov/methods/genetox/genetoxdoc/DraftRevMn30Jan07v4.pdf>

<sup>6</sup> [http://ecvam.jrc.it/ft\\_doc/ESAC26\\_statement\\_rLLNA\\_20070525-1.pdf](http://ecvam.jrc.it/ft_doc/ESAC26_statement_rLLNA_20070525-1.pdf)

<sup>7</sup> [http://iccvam.niehs.nih.gov/docs/acutetox\\_docs/guidance0801/iv\\_guide.pdf](http://iccvam.niehs.nih.gov/docs/acutetox_docs/guidance0801/iv_guide.pdf)

<sup>8</sup> [http://iccvam.niehs.nih.gov/docs/acutetox\\_docs/finalrpt/finalall0801.pdf](http://iccvam.niehs.nih.gov/docs/acutetox_docs/finalrpt/finalall0801.pdf)

Clearly, this represents another critical missed opportunity for ICCVAM as it is now seven years later, and ICCVAM has made no progress in implementing the cell-based methods even as a reduction measure and has cynically ignored their potential as a replacement measure.

Due in part to this demonstrated failure on the part of the SACATM and ICCVAM, Congress required ICCVAM to draft a five-year plan. SACATM's interpretation of the Congressional request was that SACATM and ICCVAM should "in partnership with relevant federal agencies, develop a 5-year plan that addresses the following two objectives: 1) research, development a, translation and validation of new and revised non-animal and other alternative assays for integration into federal agency testing programs and 2) identification of areas of high priority for new and revised non-animal and alternative assays..." In this regard, the Draft Plan is disappointing in its lack of direction and apparent lack of commitment to a coherent process to achieve either of its own objectives.

In addition, ICCVAM invited public comments in November 2006 and received comments from groups as varied as the American Chemical Council, private companies developing in vitro methods, and animal welfare organizations. In spite of very different agendas, these comments contained several common suggestions for a productive way forward. However, the current Draft Plan fails to incorporate or consider any of these suggestions.

Chapter 1 of the Draft Plan describes "Research, Development, Translation and Validation Activities for Priority Test Methods", and the Draft Plan states that the criteria used for setting priorities are: 1) Potential impact on reducing, refining, or replacing animals for testing, 2) Applicability to multiple agencies, and 3) Potential to provide improved prediction of adverse health or environmental effects. However, the Draft Plan provides no overview, description or analysis of priority setting for either methods under development or for planned activities. Instead, Chapter 1 contains virtually the same laundry list of methods under consideration that was presented at the SACATM meeting in November 2006, with no explanation regarding the basis upon which they were chosen, or how these methods relate to the stated priorities. For example, there is no mention in the Draft Plan of alternative approaches for reproductive or developmental toxicity testing, methods that consume far more animals than any other methods under consideration, suggesting that priority 1) listed above was not actually used as a criterion in creating the Draft Plan.

In the November solicited comments, NICEATM/ICCVAM specifically asked the following question: 1. Do you have comments on the priority areas for the development and validation of alternative test methods listed above?<sup>9</sup> In our December 2006 comments, we provided several suggestions for setting criteria and identifying needs, none of which have been incorporated into the draft Plan.<sup>10</sup>

The implicit purpose of the Appropriations Committees' request for a five-year plan was to allow NICETAM and ICCVAM to develop and articulate a new approach for the future. But Chapters 3 and 4 of the draft represent grievously abandoned opportunities. Chapter 3 provides an opportunity for NICEATM/ICCVAM to outline a specific plan for improving regulatory acceptance of validated alternative methods. Such a plan would involve agency input of regulatory endpoints requiring animal testing, specific descriptions of replacement methods, and delineation of an integrated

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<sup>9</sup> FR Doc. E6-19094 Filed 11-9-06; 8:45 am]

<sup>10</sup> <http://iccvam.niehs.nih.gov/docs/StrPlnPubCmts.htm>

validation/regulatory use process. The Draft Plan contains references to “continued” activities to interact with regulatory agencies and other stakeholders, such as “by broadly communicating the outcomes of ICCVAM review activities and/or workshops via the Federal Register, at national or international scientific meetings, via publications, and at training courses.” This approach has been demonstrably ineffective for the past decade, and there is no reason whatsoever to believe it will be more successful in the future.

Similarly, Chapter 4 provides an opportunity to articulate new approaches to achieving productive partnerships and stakeholder participation. Again, the draft Plan contains only descriptions of past approaches to developing partnerships and fostering interactions, with several promises to continue these same approaches, all of which have achieved very limited success over the past decade. The point of requesting a five-year plan is to *re-strategize*, to develop *new* approaches to *improve* and *strengthen* interactions. Again, several suggestions were provided in the animal protection community’s December 2006 comments, none of which have been incorporated into the draft Plan.

One can only conclude from this failure of the NICEATM and ICCVAM to take this opportunity to develop new approaches, and the fact that previous comments have largely been ignored, that ICCVAM has no intention of making any substantive changes to improve its thus far ineffective approach. Once again, this leads us to question ICCVAM’s commitment to both the intent and the process of its stated purposes and goals. We urge SACATM to ensure that the NICETAM and ICCVAM to take this opportunity to articulate a detailed and coherent plan for achieving its stated objectives by incorporating the comments made by the animal protection community both December 31, 2006<sup>11</sup> and June 7, 2007.

Sincerely,



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<sup>11</sup> <http://iccvam.niehs.nih.gov/docs/5YrResponses/ICCVAM5yrplanHSLF.pdf>