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Received
NICEATM
3/13/06

March 13, 2006

Dr. William S. Stokes
NICEATM Director
NIEHS
P.O. Box 12233, MD EC-17
Research Triangle Park, North Carolina 27709

RE: Federal Register Doc. E6-1019

Dear Dr. Stokes,

On behalf of both the Alternatives Research & Development Foundation (ARDF) and the American Anti-Vivisection Society (AAVS), I am submitting these comments to support the HSUS nomination for ICCVAM assessment of alternative test methods to the mouse LD50 assay for botulinum toxin potency testing.

Having been aware for some time of the efforts of the Fund for the Replacement of Animals in Medical Experiments (FRAME) in England on this topic, we are pleased to see that ICCVAM has taken the advice of its SACATM and supports with a high priority the concept of a workshop to discuss alternative methods and approaches and we welcome the opportunity to commend this effort.

Specifically, our response to your request for comments is:

1) ARDF and AAVS support and confirm the information already provided to ICCVAM in the HSUS nomination and have nothing further to add at this time.

2.) ARDF and AAVS consider that proceeding with a workshop on this topic is highly relevant to ICCVAM's mission, highly appropriate and should be a high priority. Considering the large numbers of animals affected, the suffering involved and severity of the test, the use of LD50-- a widely discredited test, and the opportunity to complement efforts by counterparts in Europe who are examining the same issue, this is an ideal candidate for prioritization by ICCVAM.

3.) Scientific experts on this topic are probably apparent from the literature citations provided by HSUS. In our experience, individuals well known to you, Coenraad Hendriksen of the Netherlands, and Robert Combes from FRAME in England, would be

excellent workshop panelists, if you could prevail upon them to participate. Of course, ARDF and AAVS have no objection to Martin Stephens from HSUS participating as well, if that is not prohibited by rules excluding nominators. If ICCVAM is interested in the most informed participants, those three could be a great asset. (I am not including contact information since these are prominent individuals; if that information is needed, please advise and I will be happy to obtain it.)

4.) ARDF and AAVS are not in possession of test data from mouse LD50, etc. However, this request affords us the opportunity to urge ICCVAM to utilize whatever tools it may have available to secure the extensive information that Botox™ manufacturer Allergan, Inc. has in its possession. Clearly, this company's documentation would be most valuable in the assessment.

In addition, this request for data affords us the opportunity to emphasize that we would only support collection of existing animal data, and not any use of animals for new data collection or validation experiments.

In closing, we would like to encourage that the workshop focus on expediting the utilization of *in vitro* alternative tests, such as the SNAP-25 assay. It would be unfortunate if the energy expended in pursuing this course resulted in merely a timid modification of protocols as is sometimes seen. We urge ICCVAM to be diligent and bold in its mission to assess and validate and reach beyond refinement.

Further, we would like to caution ICCVAM against following any tendency to validate against the existing animal test, since in this case, the LD50 is so famously unreliable and this may prove the ironic obstacle in validating a superior *in vitro* test alternative.

Thank you for this opportunity to comment on ICCVAM's consideration of the HSUS nomination and next steps. In summary, ARDF and AAVS urge ICCVAM to proceed with scheduling the expert workshop and move forward to reduce the tremendous animal suffering resulting from botulinum toxin potency testing in mice as soon as possible.

Sincerely,

Sue A. Leary
President