May 22, 2015

Dr. Warren S. Casey, Director
National Toxicology Program Interagency Center
for the Evaluation of Alternative Toxicological Methods P.O. Box 12233
Mail Drop K2-16
Research Triangle Park, NC 27709
Sent via email to warren.casey@nih.gov

Dear Dr. Casey:

The following comments are submitted on behalf of Center for Responsible Science (CRS), and SAFER Medicines Trust (SMT).

We are encouraged by ICCVAM's new direction since the appointment of Dr. Warren Casey as Director of NICEATM. Dr. Casey has maintained an "open door" policy and we appreciate the opportunity for regular interaction.

Pragmatic approach to validation

Safer Medicines Trust, with input from many senior pharmaceutical and academic scientists, has developed a novel approach to validation of new tests for the safety testing of chemicals, including medicines. The approach consists of paired drugs that have been marketed and have caused adverse events in people (positive controls) and related partners that did not cause these events (negative controls) being subjected to a range of human-focused tests to see if any or all of them can identify the toxicities that led to each withdrawal. This approach is currently being tested in a proof-of-principle study as part of the EPA ToxCast program, and is the basis of a larger Integrated Approach to Testing and Assessment proposed by a multi-partner international consortium that Safer Medicines Trust has brought together.

We would like to invite ICCVAM / NICEATM and their members to consider our approach and join the consortium in the planning and execution of a pragmatic validation of human biology-based *in vitro* and *in silico* tests, to address the current gaps in safety testing for the protection of patients and consumers. Such an approach could help to avoid the continued use of unnecessary tests (e.g. the Draize test), which is used despite the existence of validated NATMs (non-animal test methods), by more clearly demonstrating the adequacy of the NATMs and thus incentivizing their use.

Use of DRAIZE in Pharmaceutical Development

CRS approached Dr. Casey last fall regarding research we conducted regarding the use of Draize for skin and eye irritation testing for pharmaceuticals. We

discovered that 94% of all the skin irritation testing and 60% of all eye irritation testing conducted for novel new drugs approved between 2011-2014 used the Draize method. Dr. Casey invited us to present our research at an ICCVAM meeting last month so ICCVAM members could have a discussion. The ICCVAM member agencies listened to our presentation and will hopefully consider developing new analysis and approaches which allow the in vitro tests to predict mild and moderate irritation, and address how best to achieve harmonization between US agencies on the use of Draize. We appreciate ICCVAM's ongoing efforts on this issue.

We appreciate the opportunity to submit comments. We look forward to continued progress and collaboration.

Sincerely,

Katya Tsaioun, Ph.D.
Safer Medicines Trust, USA
Cambridge, MA
+1-508-812-0850
katya@safermedicines.org

Tamara Drake
Center for Responsible Science
Director of Research and Regulatory Policy
Pacific Palisades, CA
tami.drake@crs501.org