

August 28, 2012

Dr. William S. Stokes
Director, NICEATM
National Institute of Environmental Health Sciences
PO Box 12233, MS K2-16
Research Triangle Park, NC 27709



PEOPLE FOR THE ETHICAL
TREATMENT OF ANIMALS

HEADQUARTERS
501 FRONT STREET
NORFOLK, VA 23510
TEL 757-622-PETA
FAX 757-622-0457

**Re: 77 FR 43087; July 23, 2012; National Toxicology Program (NTP)
Interagency Center for the Evaluation of Alternative Toxicological Methods
(NICEATM); Nomination of an *in vitro* test method for the identification of
contact allergens: request for comments and data.**

Dear Dr. Stokes,

These comments are submitted on behalf of People for the Ethical Treatment of Animals (PETA) and the Physicians Committee for Responsible Medicine (PCRM). The parties to this submission are national animal protection and scientific advocacy organizations with a combined constituency of more than three million Americans who share the common goal of promoting reliable and relevant regulatory testing methods and strategies that protect human health and the environment while reducing, and ultimately eliminating, the use of animals.

In June, 2012, ICCVAM received a nomination from the National Institute for Occupational Safety and Health (NIOSH) to evaluate a novel *in chemico* electrophilic allergen screening assay (EASA) for the identification of electrophilic allergic contact dermatological (ACD) hazards. This nomination proposed collaboration with NICEATM to conduct validation studies and determine the most appropriate decision criteria to maximize the sensitivity and specificity of the EASA.

ICCVAM reviewed the nomination and concluded that EASA should be assigned high priority for further evaluation and proposed that the ICCVAM Immunotoxicity Working Group (IWG) and NICEATM contribute to the proposed studies by reviewing and commenting on (1) the optimization and standardization of the test method protocol, (2) the validation study design, and (3) the selection of reference chemicals for the validation study.

In light of the potential usefulness and simplicity of EASA as identified in preliminary studies, this proposal is acceptable under the condition that ICCVAM ensure that (1) reference chemicals are chosen from existing databases of chemicals for which LLNA data have already been compiled, ensuring that no new *in vivo* studies are initiated and (2) reference chemical selection and validation study design is coordinated with currently ongoing validation efforts of *in vitro* methods for detection of ACD hazards at ECVAM.

At least two published databases of LLNA data for more than 300 chemicals covering the full range of allergenic potencies are publicly available, and ICCVAM should commit to exhausting

these and other databases of historical information. **Under no circumstances should additional LLNA tests be conducted during EASA validation.**^{1,2}

ECVAM and other organizations have stressed the importance of a common set of reference chemicals during method development. Use of chemicals on a list such as that prepared by ECVAM and Cosmetics Europe (formerly Colipa) provide a valuable reference for the improvement of methods already in development while also facilitating an early comparative assessment of the performance of a method with respect to existing tests.³ This also encourages evaluation of a given method's possible contribution to a testing strategy, which is the anticipated path to development of a fully *in vitro* approach to skin sensitization testing. ICCVAM should ensure that these reference chemicals are included in any validation plans for EASA, as only two of the 23 chemicals tested in the initial demonstration of EASA are represented in ECVAM and Cosmetics Europe's suggested list of reference substances.⁴

To summarize, we support ICCVAM's efforts in this regard as long as ICCVAM evaluates the validation of EASA in an integrated fashion to help ensure the implementation of *in vitro* immunotoxicity test methods worldwide as quickly as possible.

[sincerely,
R
e Redacted]
d
a
c
Jeffrey Brown
Research Associate, Regulatory Testing Division
People for the Ethical Treatment of Animals
]

[Redacted]

Kristie Sullivan, MPH
Director, Regulatory Testing Issues
Physicians Committee for Responsible Medicine

¹ G. Gerbrick, C. Ryan, P. Kern et al. 2005. "Compilation of historical local lymph node data for evaluation of skin sensitization alternative methods." *Dermatitis*. 16(4): 157-202.

² P. Kern, G. Gerberick, C. Ryan, I. Kimber, A. APTula, and D. Basketter. 2010. "Local lymph node data for the evaluation of skin sensitization alternatives: a second compilation." *Dermatitis*. 21(1): 8-32.

³ S. Casati, P. Aeby, I. Kimber et al. 2009. "Selection of chemicals for the development and evaluation of *in vitro* methods for skin sensitization testing." *ATLA*. 37: 305-312.

⁴ I. Chipinda, R. Ajibola, M. Morakinyo et al. 2010. "Rapid and simple kinetics screening assay for electrophilic dermal sensitizers using nitrobenzenethiol." *Chemical Research in Toxicology*. 23: 918-925.