Betreff: Re: public comment to ICCVAM Expert Panel Review of in vitro methods for identifying ocular corrosives
Datum: Thu, 30 Dec 2004 19:23:01 +0100
Von: Zebet
An: Bill Stokes, Leonard Schechtman, Thomas Hartung, Ray Ticce

Dear Bill,

in response to the publication of the BRDs of the four in vitro eye irritation test on the internet on November 1, 2004, and the request for public comments, I am submitting my second comment today to meet the deadline set for the peer review process.

As you know, Dr. John Harbell (IIVS Gaithersburg MD) has submitted a second public comment dated December 28, 2004, in which he critically reviewed the inconsistent use of the definition of validation, which is the core of the current Expert Panel Review process. As you may know, as participant of the validation workshops in Amden (Switzerland) in 1990 and 1994 (Balls et al., 1990; Balls et al. 1995), I have actively been involved in developing the scientific concept of experimental validation for regulatory purposes, and I have also served as an invited expert at the ICCVAM and OECD workshops in 1995 and 1996, where an international agreement was reached on the concept and definition of experimental validation.

The participants of all of these international meetings agreed on the following definition for experimental validation "Validation is the process by which the reliability and relevance of a test methods are established for a specific purpose" (ICCVAM 1996, 2003). In the "*ICCVAM Guidance for the Nomination and Submission of New, Revised, and Alternative Test methods*" published in 2003 reliability and relevance have been defined in the following manner:

Reliability: A measure of the degree to which a test method can be performed reproducibly within and among laboratories over time. It is assessed by calculating intra- and inter-laboratory reproducibility and intralaboratory repeatability.
Relevance: The extent to which a test method correctly predicts or measures the biological effect of interest in humans and another species of interest. Relevance incorporates considerations of the "accuracy" or "concordance" of a test method.

I am now most surprise to find a different definition of "validation" as "footnote1" in the "Preface" sections of the the four BRDs (BCOP BRD pg. xxiv; ICE BRD pg. xxii; IRE BRD pg. xxiv; HET-CAM BRD pg. xxviii: "Validation is the process by which the reliability and *accuracy* of a test method are established for a specific purpose (ICCVAM 1996, 2003)". It is obvious that the word "relevance" has been replaced by the term "accuracy". This change has, of course, important implications, since the meaning of the two words is definitely not identical. According to my perception, the term "accuracy" validation is restricted to a biostatistical view while "relevance" is also covering the biological aspects a of a new test method.

As you may expect, as head of ZEBET, the National German Centre for the Documentation and Evaluation, I am most interested in achieving our common goal of getting alternative methods accepted for regulatory purposes at the international level. In order to achieve this important goal and to avoid unnecessary delay, it is important that regulatory agencies are working according to the same rules. Taking into account the agreements on defining the terms for experimental validation that we have reached at the OECD level in 1996, we have to stick to the definition of the "validation" process, which also has officially been accepted by ICCVAM and and was published in 1996 and 2003.

For the reasons given, I want to ask ICCVAM to confirm that the "official" definition of validation given in the ICCVAM "Guidelines for Submission of Alternatives test Methods" published in 1996 and 2003 has not been changed and is still "valid". If my assumption is correct, I want to ask ICCVAM and NICEATM to correct the definition of validation in the footnote of the four BRDs accordingly.

I apologize that I did not bring up this issue any earlier, since I did not read the preface carefully enough.

I hope that my comment will reach you in time to be taken into account as "public comment". If it is too late, I would be happy, if you accept my submission as a comment of one of the "Expert reviewers" of the IRE BRD.

With the best regards
Sincerely
Horst Spielmann

--
Dr. med. Horst Spielmann
Direktor und Professor
Head of Dept. "Scientific Services"
and Head of ZEBET

ZEBET at the BfR
Diedersdorfer Weg 1
D-12277 Berlin
Tel: +49-1888-412-2270
Fax: +49-1888-412-2958
email: zebet@bfr.bund.de & spielmann.zebet@bfr.bund.de

ZEBET http://www.bfr.bund.de/cms/detail.php?id=1591
Zentralstelle zur Erfassung und Bewertung von
Ersatz-und Ergaenzungsmethoden zum Tierversuch
(National German Centre for the Documentation and
Evaluation of Alternatives to Testing in Animals)

BfR http://www.bfr.bund.de/cms/detail.php?template=internet_en_index_js
Bundesinstitut fuer Risikobewertung
(Federal Institute for Risk Assessment)

Please visit the website of the 5th World Congress on
Alternatives & Animal Use in the Life Sciences
August 21-25, 2005 in Berlin, Germany
http://www.ctw-congress.de/act2005/