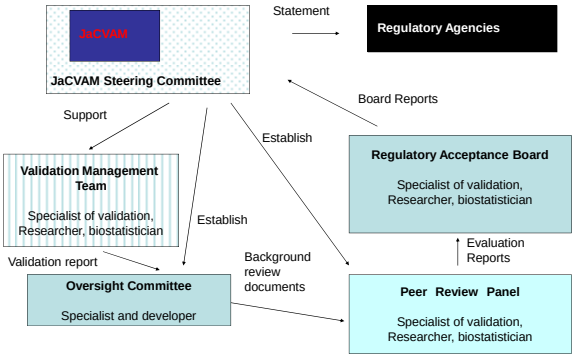
JaCVAM's role on new alternatives to animal testing and International harmonization

Kojima, H., Inoue, T. and Ohno, Y.; National Institute of Health Sciences (NIHS)

Introduction

In November 2005, the Japanese Center for the Validation of Alternative Methods (JaCVAM) was established as part of the Division of Pharmacology, National Center for Biological Safety and Research, National Institute of Health Sciences (NIHS) in Japan. JaCVAM's roles are to facilitate the validation of alternative methods developed in Japan for safety evaluation, to conduct peer review of alternative methods, and to promote practice of the 3Rs in the area of animal testing in Japan.
It is important for JaCVAM to cooperate with other VAMs in the framework of the International Cooperation on Alternative Test Methods (ICATM). JaCVAM will contribute ICVAM for enhanced international cooperation, collaboration and communication with the European Centre for the Validation of Alternative Methods (ECVAM), the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) / the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and Health Canada.
JaCVAM have a regulatory acceptance board to discuss on the validity of new or revised methods for regulatory purpose. This board reviews reports of new or revised ones prepared by peer review panel and make statements on the test methods for regulatory agency.



Framework for Validation, Peer Review and Regulatory Acceptance of Alternative Methods in Japan

JaCVAM Regulatory Acceptance Board

No	Name	Affiliation
1*	Toru Inoue	National Institute of Health Sciences
2	Yoshiaki Ikarashi	National Institute of Health Sciences
3	Yuko Okamoto	Japan Cosmetic Industry Accosiation
4	Hiroshi Onodera	Pharmaceuticals and Medical Devices Agency
5	Noriho Tanaka	Hatano Research Institute Food and Drug Safety Center
6	Kazuichi Nakamura	Japan Pharmaceutical Manufacturers Association
7	Takeyuki Oshima	Japan Chemical Industry Association
8	Iku Mitta	Pharmaceuticals and Medical Devices Agency
9	Hiroo Yokozeki	Tokyo Medical and Dental University
10	Midori Yoshida	National Institute of Health Sciences
11	Takemi Yoshida	Showa University
12	Isao Yoshimura	Tokyo University of Science

* Chair

Validation study

On-going study
Skin sensitisation: h-CLAT assay (ECVAM/JaCVAM)

Genotoxicity: In vivo/in vitro Comet assay (ICCVAM/ECVAM/JaCVAM)

Endocrine disrupter screening: Stably Transfected Transcriptional Activation (STTA) antagonist assay (JaCVAM)

Endocrine disrupter screening: CCi assay (ICCVAM/KoCVAM/JaCVAM)

Bhras cell transformation assay (ICCVAM/ECVAM/JaCVAM)

Eye irritation: Short Time Exposure (STE) assay (JaCVAM)

Phototocxicity : Reactive oxygen species (ROS) assay (JaCVAM)

Peer review

On-going
Skin irritation — LabCyte EPI-MODEL (Japanese)

Eye irritation — Cytotoxicity assays (SIRC or MATREX: Japanese)

Regulatory acceptance

Accepted
Bovine Corneal Opacity and Permeability (BCOP) test method for Identifying ocular corrosives and severe Irritants (Accepted on December, 2009)

Isolated Chicken Eye (ICE) for identifying ocular corrosives and severe Irritants (Accepted on December, 2009)

In vitro skin irritation testing EPISKIN (Accepted on March, 2010)

Skin Sensitization: LLNA:BrdU-ELISA (Accepted on May, 2010)

Conclusion

At 2008-2010 at the National Institute of Health Sciences (NIHS), Tokyo, Japan, the members of the JaCVAM Regulatory Acceptance Board unanimously endorsed the following statement:
1) 1) Vitrolife-Skin™, a 3-dimensional cultured skin model can be used for distinguishing between corrosive and non-corrosive chemicals
2) LLNA (Local Lymph Node Assay) :DA can be used for distinguishing between sensitizer and non-sensitizer chemicals
3) Bovine Corneal Opacity and Permeability (BCOP) test method for Identifying ocular corrosives and severe Irritants
4) Isolated Chicken Eye (ICE) for identifying ocular corrosives and severe Irritants
5) *In vitro* skin irritation testing EPISKIN for distinguishing between skin irritation and non-irritant chemicals

We are preparing a few new statements now. We will continue for many years to publish these statements and work on the regulatory agencies. We are showing these statements to the public on JaCVAM web site.

On-going
Pyrogenecity — Five *in vitro* assays (ICCVAM& ECVAM)

Acute toxicity testing — 3T3/NRU (ICCVAM)

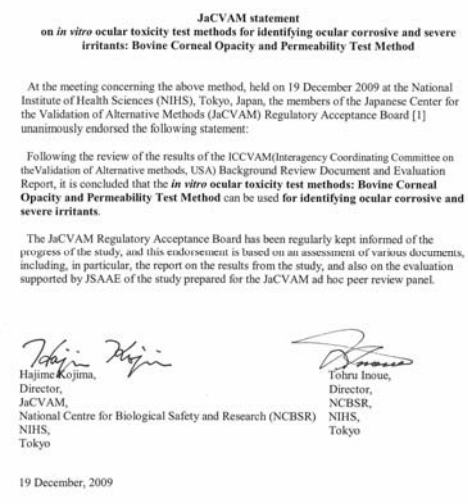
Japanese Correlation with draft OECD test guideline

New accepted TG for a Stably Transfected Transcriptional Activation (STTA) Assay for the detection of estrogenic activity of chemicals (accepted by April, 2009)

TG 429a, b: Skin Sensitisation for a Non-Radioisotope version of the Local Lymph Node Assay (LLNA:DA, LLNA:BrdU-ELISA accepted by March, 2010)

On-going
Project 4.26: Cell Transformation Assay using Balb/c 3T3 cell line
Project 4.34: EDTA Activity - New TG for a stably Transfected Transcriptional Activation (STTA) Assay for the detection of anti-estrogenic activity of chemicals
Project 4.35: New TG for an *In Vitro* Skin Irritation Assay (LabCyte model)
Project 4.36: New TG: Comet Assay in Genotoxicity Testing
Project 4.??: Bhras cell transformation assay

JaCVAM statements in 2009-2010



JaCVAM statement
on *in vitro* ocular toxicity test methods for identifying ocular corrosive and severe irritants: Bovine Corneal Opacity and Permeability Test Method

At the meeting concerning the above method, held on 19 December 2009 at the National Institute of Health Sciences (NIHS), Tokyo, Japan, the members of the Japanese Center for the Validation of Alternative Methods (JaCVAM) Regulatory Acceptance Board [1] unanimously endorsed the following statement:

Following the review of the results of the ICCVAM(Interagency Coordinating Committee on theValidation of Alternative methods, USA) Background Review Document and Evaluation Report, it is concluded that the ***in vitro* ocular toxicity test methods: Bovine Corneal Opacity and Permeability Test Method** can be used **for identifying ocular corrosive and severe irritants**.

The JaCVAM Regulatory Acceptance Board has been regularly kept informed of the progress of the study, and this endorsement is based on an assessment of various documents, including, in particular, the report on the results from the study, and also on the evaluation supported by JSAAE of the study prepared for the JaCVAM ad hoc peer review panel.

Hajime Kojima, Director, JaCVAM, National Centre for Biological Safety and Research (NCBSR) NIHS, Tokyo

Tohru Inoue, Director, NCBSR, NIHS, Tokyo

19 December, 2009

- MHLW (Ministry of Health, Labour and Welfare)
- 厚生労働省 Ministry of Health, Labour and Welfare
- METI (Ministry of Economy, Trade and Industry)
- MOE (Ministry of Environment)
- MAFF (Ministry of Agriculture, Forestry and Fisheries)