“Japanese activities for alternative to animal testings around the world”

Hajime Kojima,
NIHS

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1. Background
2. OECD activities
3. Japanese activities
4. International cooperation
5. Asian cooperation
EU bans sale of all animal-tested cosmetics

A complete ban on the sale of cosmetics developed through animal testing has taken effect in the EU.

The ban applies to all new cosmetics and their ingredients sold in the EU, regardless of where in the world testing on animals was carried out.

The 27 EU countries have had a ban on such tests in place since 2009. But the EU Commission is now asking the EU's trading partners to do the same.

Animal rights lobbyists said EU officials had "listened to the people".

The anti-vivisection group BUAV and the European Coalition to End
CONNECTING THE DOTS FOR ANIMALS:
HISTORY OF THE EU BAN ON ANIMAL TESTING FOR COSMETICS

- 1993: First EU provisions (directive) on marketing, BAN of cosmetics tested on animals. Deadline for BAN: 1998

- 1997: EU Directive postponing the BAN deadline until 2003 because of the lack of alternatives to animal testing

- 2003: BAN of animal testing of finished cosmetic products enters into force in the EU

- 2004: BAN of marketing of finished cosmetic products tested on animals

- 2007: BAN of marketing of cosmetic ingredients tested on animals

- 2009: BAN of marketing of finished cosmetic products tested on animals enters into force in the EU. The BAN of marketing of cosmetic ingredients tested on animals enters into force in the EU. The BAN still allowed for the most complex human health effects, e.g., cancer, allergens.


EU FUNDING ON RESEARCH ON ALTERNATIVES TO ANIMAL TESTING IN 2007-2011: €238 MILLION
## Cosmetic regulation and animal testings

<table>
<thead>
<tr>
<th>Country</th>
<th>Update</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU</td>
<td>Prohibition</td>
<td>Products and ingredients</td>
</tr>
<tr>
<td>Israel</td>
<td>Prohibition</td>
<td>Products and ingredients</td>
</tr>
<tr>
<td>India</td>
<td>Prohibition</td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Abolishment of animal testings</td>
<td>Excluding specific cosmetic</td>
</tr>
<tr>
<td>Brazil</td>
<td>Submitting the bill</td>
<td>Prohibition on Sao Paulo State</td>
</tr>
<tr>
<td>USA</td>
<td>Submitting the bill</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>Submitting the bill</td>
<td></td>
</tr>
<tr>
<td>South Korea</td>
<td>No requests</td>
<td>Excluding functional cosmetics</td>
</tr>
<tr>
<td>Japan</td>
<td>No requests</td>
<td>Excluding Quasi-drug</td>
</tr>
</tbody>
</table>
About the OECD

❯ Who does what
❯ What we do and how
❯ Members and partners
❯ History
❯ Budget
❯ Publishing
❯ Careers at the OECD

It's all about people: Jobs, Equality and Trust
APPLY INTEGRATED APPROACHES TO TESTING AND ASSESSMENT

All of the work on alternative methods is undertaken at the OECD with the objective of contributing to more integrated approaches to testing and assessment. In practice, integrated approaches, which take into account the tools outlined above, are used in the OECD Existing Chemicals Programme which generates internationally agreed initial hazard assessments of chemicals.

This practical application of integrated approaches improves their regulatory acceptance and facilitates their implementation into national and regional chemical assessment schemes in OECD member countries.

AVOID DUPLICATION OF TESTING

The OECD Mutual Acceptance of Data (MAD) framework has had a major impact on testing practices. MAD guarantees that data generated in the testing of chemicals in an OECD member country, or adhering non-member country, in accordance with OECD Test Guidelines and OECD Principles of Good Laboratory Practice shall be accepted in other member or adhering countries for purposes of chemical assessment and other uses relating to the protection of man and the environment. This proactive framework saves thousands of animals every year and its impact increases as non-OECD economies join the MAD system.

Furthermore, the OECD has developed the Global Portal to Information on Chemical Substances (eChemPortal). eChemPortal offers free public access to information on properties of chemicals through a simultaneous search of multiple databases, thereby improving the access to existing test results and reducing the risk of unnecessary testing.

WHERE CAN I FIND OECD TOOLS RELATED TO CHEMICAL SAFETY AND ANIMAL WELFARE?

(Q)SARs, Grouping of Chemicals and the (Q)SAR Application Toolbox

www.oecd.org/env/existingchemicals/qaar

Test Guidelines, in vitro test methods, molecular screening and toxicogenomics

www.oecd.org/env/testguidelines

Integrated Approaches to Testing and Assessment

www.oecd.org/env/existingchemicals

Mutual Acceptance of Data

www.oecd.org/env/glp

Global Portal to Information on Chemical Substances

www.oecd.org/ehs/eChemPortal

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Cathy Imagawa, 2006
KayYann-Fotolia.com

© OECD 2009
For more information contact the OECD Secretariat at
ehscont@oecd.org

www.oecd.org/env/ehs
A global outreach

OECD Member Countries  (34)
Countries/Economies Engaged in Working Relationships with the OECD
Functioning of the Programme

• Work plan includes projects lead by member countries, updated and declassified annually.
• SPSF template for project proposal, available to NCs, concerns projects on:

<table>
<thead>
<tr>
<th>New Test Guideline</th>
<th>Guidance document</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revised Test Guideline</td>
<td>Detailed Review Paper</td>
</tr>
<tr>
<td>Deletion of an existing Test Guideline</td>
<td>Other, specify:</td>
</tr>
</tbody>
</table>

• Regulatory need
• Animal welfare main motivations
• Cost effectiveness for projects
Table. OECD Test Guidelines for *in vitro* test method (2015)

<table>
<thead>
<tr>
<th>Class</th>
<th>Test methods</th>
</tr>
</thead>
</table>
| Corrosion              | *In vitro* Skin Corrosion: Transcutaneous Electrical Resistance Test Method (TER) : TG430  
|                        | *In vitro* Skin Corrosion: Reconstructed Human Epidermis (RHE) test method : TG431  
|                        | CORROSITEX Skin Corrosivity Test : TG435                                      |
| Skin irritation         | *In vitro* Reconstructed Human Epidermis (RHE) Test methods, EpiDerm, EPISKIN, SkinEthic, LabCyte EPI-Model: TG439 |
| Phototoxicity          | 3T3 NRU Phototoxicity Test : TG432                                             |
| Eye irritation          | Bovine Corneal Opacity and Permeability Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage: TG437 |
|                        | Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage: TG438 |
|                        | Fluorescein Leakage Test Method for Identifying Ocular Corrosives and Severe Irritants: TG460 |
|                        | Short Time Exposure In Vitro Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage: TG491 |
|                        | Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage: TG492 |
| Skin sensitisation     | *In Chemico* Skin Sensitisation, Direct Peptide Reactivity Assay (DPRA) : TG442C |
|                        | *In Vitro* Skin Sensitisation, ARE-Nrf2 Luciferase Test Method : TG442D        |
| Endocrine disrupter screening | Performance-Based Test Guideline for Stably Transfected Transactivation In Vitro Assays to Detect Estrogen Receptor Agonists and Antagonists: TG455  
|                        | H295R Steroidogenesis Assay : TG456                                           |
|                        | BG1Luc Estrogen Receptor Transactivation Test Method for Identifying Estrogen Receptor Agonists and Antagonists: TG457 |
|                        | Performance-Based Test Guideline for Human Recombinant Estrogen Receptor (hrER) In Vitro Assays to Detect Chemicals with ER Binding Affinity : TG493 |
| Genotoxicity           | Bacterial Reverse Mutation Test : TG471                                       |
|                        | *In vitro* Mammalian Chromosome Aberration Test : TG473                        |
|                        | *In Vitro* Mammalian Cell Gene Mutation Tests using the HpRt and xprt genes : TG476 |
|                        | *In vitro* Micronucleus Test : TG487                                            |
|                        | *In Vitro* Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene : TG490 |
| Skin absorption        | Skin Absorption: *In vitro* Method : TG428                                     |
Japanese activities
OECD Test Guidelines developed by Japan

- Skin sensitization assay, LLNA : DA, TG 442A (2010)
- Skin sensitization assay, LLNA : BrdU-ELISA , TG 442B (2010)
- Skin irritation assay with LabCyte EPI-MODEL 24, TG 439 (2013)
- In vivo comet assay TG 489 (2014)

✓ Performance-based Test Guideline for stably transfected transactivation in vitro assays to detect estrogen receptor agonists and antagonist, Revised TG 455 (2015)

✓ Short time exposure (STE) assay for eye irritation testing TG490 (2015)

✓ Bhas 42 cell transformation assay (2016) Guidance document

✓ h-CLAT assay for skin sensitisation testing (2016)

✓ Stable transfected transcriptional activation (STTA) assay for androgen disruptor screening (AR-Ecoscreen)(2016)
Test Method Evolution and Translation Process: Concept to Implementation

**Stage**

- **Review Risk Assessment Methods**
  - Identify need for new, improved and/or alternative test methods

- **Research**
  - Investigate toxic mechanisms; identify biomarkers of toxicity

- **Development**
  - Incorporate biomarkers into standardized test method

- **(Pre) Validation**
  - Optimize transferable test method protocol

- **Validation**
  - Determine relevance and reliability

- **Peer Review**
  - Independent scientific evaluation of validation status

- **Acceptance**
  - Determine acceptability for regulatory risk assessment

- **Implementation**
  - Effective use of new methods by regulators and users
JaCVAM: Japanese Center for the Validation of Alternative Methods

This Center was established at the National Institute of Health Sciences (NIHS) in Japan, 2005 by the Ministry of Health, Labour and Welfare (MHLW).

JaCVAM’s Goals

• To promote the 3Rs in animal experiments for the evaluation of chemical substance safety in Japan.
• To establish guidelines for new alternative experimental methods through international collaboration.
JaCVAM roles

• JaCVAM assesses the utility, limitations, and suitability for use in regulatory studies of test methods for determining the safety of chemicals and other materials and also performs validation studies when necessary. In addition, JaCVAM cooperates and collaborates with similar organizations in related fields, both in Japan and internationally.

• JaCVAM activities are also beneficial to application and approval for the manufacture and sale of pharmaceutical chemicals, pesticides and other products as well as to revisions to standards for cosmetic products.
<table>
<thead>
<tr>
<th>Classification</th>
<th>Test name</th>
<th>Validation study</th>
<th>Peer review</th>
<th>Regulatory acceptance</th>
<th>Recommendation to government</th>
<th>OECD</th>
<th>Collaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Corrosivity test</td>
<td>(1) Reconstructed human tissue test made in Japan: Vitrolife-Skin</td>
<td>Feb-09</td>
<td>Jun-08</td>
<td>Jun-08</td>
<td>Aug-08</td>
<td>Guideline No.431</td>
<td>JSAAE</td>
</tr>
<tr>
<td>02 Phototoxicity test</td>
<td>(1) 3T3—NRU</td>
<td>BfR Nov-04</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) Yeast growth inhibition phototoxicity assay and the red blood cell photohemolysis assay</td>
<td>Jan-09</td>
<td>May-09</td>
<td>on going</td>
<td>Guideline No.432</td>
<td>JSAAE</td>
<td></td>
</tr>
<tr>
<td>03 Skin sensitization test</td>
<td>(1) LLNA-DA</td>
<td>Jun-07</td>
<td>Feb-08</td>
<td>Oct-08</td>
<td>Nov-08</td>
<td>JSAAE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) LLNA-BrdU</td>
<td>Aug-08</td>
<td>Feb-09</td>
<td>on going</td>
<td></td>
<td>JSAAE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3) i-CLAT</td>
<td>start in 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(4) LLNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(5) rLLNA</td>
<td>ECVAM, ICCVAM</td>
<td>start in 2009</td>
<td></td>
<td></td>
<td>ICCVAM</td>
<td></td>
</tr>
<tr>
<td>04 Skin irritation test</td>
<td>(1) Reconstructed human tissue test</td>
<td>ECVAM</td>
<td>Nov-08</td>
<td>on going</td>
<td>Draft test guideline</td>
<td>ECVAM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) Reconstructed human tissue test made in Japan</td>
<td>May-09</td>
<td></td>
<td></td>
<td></td>
<td>JSAAE</td>
<td></td>
</tr>
</tbody>
</table>

Note: MJM
Test methods under the OECD work plan

- IL-8 Luc assay for skin sensitisation testing
- ROS assay for phototoxicity testing
ICH HARMONISED TRIPARTITE GUIDELINE

Guideline on Photosafety Evaluation of Pharmaceuticals S10 (Step 4 Version: 2013)

**ROS** (Reactive oxygen species) assay including superoxide anion and singlet oxygen approved in the guideline.
Japan organized **on-going** International peer review

1. SIRC-CVS assay for eye irritation testing
2. Vitrigel-EIT for eye irritation testing (supported by MAFF)
3. LabCyte Cornea-mode EIT for eye irritation testing (supported by JSAAE)
Japan organized **on-going** International validation studies

1. Hand-1 Luc EST for developmental screening (supported by METI)

2. MITA for immunotoxicity screening

3. ADRA for skin sensitisation testing
**Summary**

*In vitro* test methods are considered necessary for regulatory within merits and demerits that can be characterized as follows:

1) *In vitro* test methods are useful for hazard identification but not for risk assessment, with the exception of *in vitro* skin absorption assays (dose-response, exposure route, etc.). For example, the *in vitro* skin irritation method (TG 439)\(^{14}\) provides an *in vitro* procedure that may be used for hazard identification of substances and mixtures classified as UN GHS Category 2 (irritants). TG 439 can also be used to identify chemicals classified as No Category, provided that there is no need to identify the optional UN GHS Category 3 (mild irritants).

2) *In vitro* test methods are likely not to be sufficient as a stand-alone method to evaluate the toxic potential of chemicals based on the activation of pathways.

3) Combinations of *in silico, in chemico, in vitro* and other alternative methods within Integrated Approaches to Testing and Assessment (IATA)\(^{18}\) will be needed to substitute for the animal tests currently in use for specific Adverse Outcome Pathway (AOP)\(^{18}\) mechanistic coverage.
Regulation on Animal Welfare in Japan

Ministry of Environment
「 Act on Welfare and Management of Animals 」 (2007)

Standards relating to the care and management, etc.
of experimental animals (2008)

Basic principle of animal experiments in three Ministries

MEXT 2008
Animal care and rule of animal experiments for laboratories at a university

MHLW 2008
Animal care and rule of animal experiments for research institute under MHLW

MAFF 2008
Animal care and rule of animal experiments for research institute under MAFF

Principle of 3Rs
MHLW Evaluation and Licensing Division publicized the availability of alternative test methods for use in safety evaluations of cosmetics and quasi-drugs in 2012 to 2015.

<table>
<thead>
<tr>
<th>No.</th>
<th>Test Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Guidance for skin sensitization testing, LLNA</td>
</tr>
<tr>
<td>2</td>
<td>Guidance for alternative to phototoxicity testing, \textit{in vitro 3T3 NRU}</td>
</tr>
<tr>
<td>3</td>
<td>Guidance for skin sensitization testing, LLNA : DA</td>
</tr>
<tr>
<td>4</td>
<td>Guidance skin sensitization testing, LLNA : BrdU-ELISA</td>
</tr>
<tr>
<td>5</td>
<td>Guidance for alternative to eye irritation testing, BCOP</td>
</tr>
<tr>
<td>6</td>
<td>Guidance for eye irritation, the revised TG405</td>
</tr>
<tr>
<td>7</td>
<td>Guidance for alternative to eye irritation testing, ICE</td>
</tr>
</tbody>
</table>
International cooperation
The ICCR is an international group of regulatory authorities from Canada, the European Union, Japan, and the United States. ICCR members work together to promote regulatory alignment, in order to maximize consumer protection while minimizing barriers to trade. Here's where to find information on ICCR:
ICCR activities

- At ICCR 5 in 2011, a report on *Applicability of Animal Testing Alternatives in Regulatory Frameworks within ICCR Regions* described processes and proposed mechanisms in each jurisdiction for regulatory acceptance of the use of alternative methods in the area of cosmetics.

- At ICCR 6 in 2012, an overview was provided on the potential application of Quantitative Structure Activity Relationship (QSAR) prediction models for the safety assessment of cosmetic ingredients. Thereafter, it was agreed that “QSAR/in silico” computational toxicology be added to the ICCR Agenda, and a new working group was formed to further explore *in silico* models applicable to personal care products. The working group presented its report, “*In silico* Approaches for Safety Assessment of Cosmetic Ingredients” at ICCR 8 in 2014, when it was agreed that QSAR/ *in silico* should remain on the ICCR Agenda.

- The ICCR Steering Committee (SC) requested the WG to develop a draft Terms of Reference (ToR) that will be provided to the SC for input. The WG will also provide an update of activities at the ICCR-10 meeting in July, 2016.
Table 2 QSARs models for skin sensitisation

<table>
<thead>
<tr>
<th>Model</th>
<th>Type</th>
<th>Chemical coverage</th>
<th>Availability</th>
<th>Endpoint predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative alkylation index (RAI) approach</td>
<td>Local QSAR approach</td>
<td>Various RAI derived for specific chemical classes e.g. sulfonate esters, sulfones, primary alkyl bromides, acrylates, aldehydes and diketones</td>
<td>Published in the literature</td>
<td>Most of the RAI models aim to predict the EC3 value in the LLNA, a few predict the outcome in guinea pig tests</td>
</tr>
<tr>
<td>QMM approach which is an extension of the RAI approach</td>
<td>Local QSAR approach</td>
<td>Developed on the basis of Reaction mechanistic domains (Schiff base formers, Michael addition, Acylating agents, SN2)</td>
<td>Published in the literature</td>
<td>EC3 in the LLNA</td>
</tr>
<tr>
<td>Various e.g. Estrada et al., (2003)</td>
<td>Global models</td>
<td>Mainly based on the Gerberick et al (2005) dataset hence cover a broad coverage of chemicals</td>
<td>Variable</td>
<td>Potency categorisation as defined by EC3 values in the LLNA</td>
</tr>
<tr>
<td>TOPKAT</td>
<td>Expert system (statistical)</td>
<td>Based mainly on the datasets published by Cronin and Basketter (1994) hence reasonably broad coverage of chemicals</td>
<td>Commercial</td>
<td>Binary model to predict likelihood of sensitisation and additional model to estimate qualitatively the potency as defined in the GPMT</td>
</tr>
<tr>
<td>MCASE suite of models to predict each of the KEs in the AOP</td>
<td>Expert system (statistical)</td>
<td>Broad coverage of chemicals</td>
<td>Commercial</td>
<td>Models to predict the outcome of the DPRA, ARE activation, n-CLAT, EC3 potency bands and overall binary sensitisation outcome</td>
</tr>
<tr>
<td>Derek Nexus</td>
<td>Expert system (Knowledge based)</td>
<td>Broad coverage of chemicals</td>
<td>Commercial</td>
<td>Qualitative likelihood of skin sensitisation potential</td>
</tr>
<tr>
<td>TIMES-SS</td>
<td>Expert system (Hybrid)</td>
<td>Broad coverage of chemicals</td>
<td>Commercial</td>
<td>Based on data from LLNA, GPMT and Human</td>
</tr>
</tbody>
</table>
Statement of Principle for VICH – Alternatives to Animal Testing

At its 19th meeting on 23-24 January 2007 in Washington D.C., USA, the VICH Steering Committee reiterated its ambition to minimise animal testing and specifically expressed its support for the 3Rs principle – replacement, refinement and reduction of animals in research.

VICH has always striven to eliminate repetitious and unnecessary testing through harmonisation of regulatory requirements for the registration of veterinary products, a goal that undoubtedly leads to a reduction in the number of animals used for product development and registration.

While the validation of alternative testing protocols falls outside the remit of VICH, the Steering Committee recognises that the international status and influence of VICH provide a unique opportunity to encourage the use of validated alternative methods. To this end, Expert Working Groups developing guidelines involving animal experimentation have a specific responsibility to consider animal welfare, and particularly the possibilities for replacement, refinement and reduction of animal testing.
ICH Harmonised Tripartite Guideline

3. RECOMMENDATIONS FOR IN VITRO TESTS ................................................................. 5
   3.1 Test Repetition and Interpretation ................................................................. 5
   3.2 Recommended Protocol for the Bacterial Mutation Assay ......................... 5
       3.2.1 Selection of Top Dose Level ................................................................. 5
       3.2.2 Study Design/Test Protocol ................................................................. 5
   3.3 Recommended Protocols for the Mammalian Cell Assays ......................... 6
       3.3.1 Selection of Top Concentration ............................................................. 6
       3.3.2 Study Design/Test Protocols ................................................................. 6
       3.3.3 Positive Controls ................................................................................... 7
ICH S5(R3) Expert Working Group Meeting

Workpackages

Integrated testing strategies for EFD (Embryonic and Fetal Development study)
- Design of optional integrated testing strategies involving an in vivo mammalian EFD assessment and in vitro, ex vivo and non-mammalian in vivo (e.g. zebrafish) EFD assays
- Identification of scenarios of use and the limited circumstances under which such a testing strategy would be considered.

Combinations of studies –JPMA&MHLW/PMDA
- Delineate options of combining reproductive toxicity studies and their designs
- Describe the circumstances under which the outcome of preliminary EFD studies could determine the ultimate risk assessment for EFD
- Identification of scenarios of use of the different combinations

Proposed Next Steps and Timelines
✓ EWG face-to-face at June 2016 ICH Meeting is requested
✓ Timeline for Step 2a Document by June 2017
✓ A total period of 4.5 years is foreseen for Step 4 from the establishment of the EWG
✓ Public comments incorporated into Step 4 Document June 2019
ICATM

ICATM is a voluntary international cooperation of national organizations: Canada, the European Union, Japan, South Korea, and the United States.
## Comparison with VAMs

<table>
<thead>
<tr>
<th>Organization</th>
<th>Formal Name</th>
<th>Mother organization</th>
<th>Act</th>
<th>Establish.</th>
<th>Member No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>JaCVAM</td>
<td>Japanese Center for the Validation of Alternative Methods</td>
<td>National Institute of Health Sciences (NIHS)</td>
<td>None</td>
<td>2005.11</td>
<td>5(2)</td>
</tr>
<tr>
<td>KoCVAM</td>
<td>Korean Center for the Validation of Alternative Methods</td>
<td>Korean Food and Drug Association (KFDA)</td>
<td>??</td>
<td>2009.11</td>
<td>6(2)</td>
</tr>
<tr>
<td>ICATM</td>
<td>International Cooperation on Alternative Test Methods</td>
<td>None</td>
<td></td>
<td>2009.4</td>
<td></td>
</tr>
</tbody>
</table>
ICATM Members

- ICATM founded 27 April 2009 (JaCVAM, NICEATM, ECVAM, Health Canada)
- KoCVAM (Republic of Korea's Centre for the Validation of Alternative Methods) became the fifth member March 8, 2011, Washington DC

The addition of KoCVAM complements the capacities of ICATM
ICATM Purpose

• Promote consistent and enhanced voluntary international cooperation, collaboration and communication among validation organizations in order to:
  – Further optimal design and conduct of validation studies
  – Further high quality independent reviews with opportunity for stakeholder involvement
  – Enhance likelihood of harmonized recommendations on usefulness and limitations of test methods for regulatory use
  – Achieve greater efficiency by avoiding duplication of effort
  – Support timely adoption of alternative methods
ICATM Cooperation

- ICCVAM
- ECVAM
- JaCVAM
- KoCVAM

Test Method Validation Studies

Independent Peer Review of Test Method Validation Status

Development of Harmonized Test Method Recommendations

Regulatory Acceptance

International Acceptance

[Flags for USA, Canada, Europe, Japan, and Korea]
International Cooperation

2015 KoCVAM-JaCVAM Meeting

KoCVAM-JaCVAM meeting
August 23, 2015, Seoul, Korea
Shared JaCVAM’s experience of proposing ATMs and making them adopted as OECD test guidelines

Enhance cooperation among Asian countries in the field of ATMs
EPiTRI-SIT human epidermis model
Jun 10, 2015
Information of Asian Congress 2016

Jun 5, 2015
Communication from the European Commission on the European Citizens' Initiative "Stop Vivisection"

May 30, 2015
Nominations for The 2015 Lush Prize opened.

Feb 3, 2015
Recruitment of "8th Mandom International Research Grants on Alternative to Animal Experiments" was finished. Thank you for much application.

Nov 25, 2014
“Program of the 27th annual meeting was posted.”

Sept 3, 2014
Purpose and history of JSAAE

“Promote and propagate of 3Rs in Japan in research, development, and education”

- 1982: Established as a research group
  (Representatives: Prof. Tsutomu Sugawara)
- 1986: Alternative animal test investigation task force at JCIA
- 1990: Reformed to become Scientific Association
- 2002: Accepted as a member society by Science Council of Japan.
  (2005: 3Rs were officially included in the animal protection law)
  (2006: JaCVAM at NIHS)
- 2007: Organized WC6 in Tokyo

*28 times of annual meeting
General services

1) Annual meeting of the society
2) Extraordinary symposium and workshops
3) Publication
   ▶ J. Alternatives to Animal Experiments (AATEX)
   ▶ News letters (in Japanese)
   ▶ Home page
4) Financial support to related research
5) Validation and evaluation of new alternatives
6) Collect relevant information
7) Communication with other countries
8) Others
   ▶ Support of International meeting
   ▶ Collaboration with the other scientific associations
      Tissue culture Assoc, Mutagenicity assoc., etc
   ▶ Communication with animal protection group
International communication

Have been trying to set collaboration with EU and USA etc.

- Memorandum with EUSAAT: European Society For Alternatives To Animal Testing (2015)
Asian Cooperation
International communication with China

Have been trying to set collaboration with Asian countries.

• Memorandum with KSAAE: Korean Society of Alternative to Animal Experiments (2008-)
• Memorandum with Chinese society of animal experiments (2008-2012)
• Hopefully, communicate with Chinese society of Toxicity Testing and Alternatives (TTA) and Chinese society of Toxicological Laternative and Translational Toxicology (TATT)
Asian Congress 2016 on Alternatives and Animal Use in the Life Science
Outline on Asian Congress 2016

Formal Name: Asian Congress 2016 on Alternatives and Animal Use in the Life Science (Joint Meeting with 29th JSAAE Annual meeting)

Data: November 15-18, 2016

Venue: Karatsu Civic Hall in Karatsu, Saga, Japan
        Kyushu University in Fukuoka, Japan

Host: Japanese Society for Alternatives to Animal Experiments (JSAAE) under the Patronage of Alternatives Congress Trust (ACT)

Support: Human Society International (HSI), Japanese Center for the Validation of Alternative Methods (JaCVAM), Japan Cosmetic Center (JCC)
Purpose

The Asian Congress will be the first conference of its kind for researchers from Asia, and will afford an opportunity for promoting alternative methods to researchers in these places, where the concept of the Three Rs is just now achieving penetration. The Asian Congress is intended to achieve multiple missions, which will include disseminating information not just on the latest advances in including pure sciences but on practical applications of the Three Rs worldwide.
<table>
<thead>
<tr>
<th>Time</th>
<th>Nov. 16 (Tue)</th>
<th>Nov. 17 (Tue)</th>
<th>Nov. 18 (Tue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30</td>
<td>Asian Congress on Alternatives and Animal Use in the Life Sciences at Karatsu Civic Hall</td>
<td>Joint with the 29th JFRAE Annual Meeting at Convention Hall Toyota University</td>
<td>8:30</td>
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<tr>
<td>9:00</td>
<td>Welcome Address</td>
<td>Plenary lecture 3</td>
<td>Short Presentation for Poster at Room A (Main Hall)</td>
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<tr>
<td>10:00</td>
<td>Plenary lecture 1</td>
<td>Symposium 5</td>
<td>Poster Presentation at Poster room (Hall 1-3) (Even Number)</td>
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<tr>
<td>11:00</td>
<td>Plenary lecture 2</td>
<td>Young Scientist Award</td>
<td>Poster Viewing at Poster room (Hall 1-3)</td>
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<tr>
<td>12:00</td>
<td>Lunch Seminar</td>
<td>Lunch Seminar</td>
<td>Announcement of Poster</td>
</tr>
<tr>
<td>13:00</td>
<td>Symposium 1</td>
<td>Symposium 2</td>
<td>Poster Viewing at Poster room (Hall 1-3)</td>
</tr>
<tr>
<td>14:00</td>
<td>Symposium 3</td>
<td>Symposium 4</td>
<td>Award Ceremony</td>
</tr>
<tr>
<td>15:00</td>
<td>Social Tour</td>
<td>Poster Presentation at Poster room (Hall 1-3) (Odd Number)</td>
<td>Closing Ceremony</td>
</tr>
<tr>
<td>16:00</td>
<td>Welcome Party</td>
<td>Gala Dinner</td>
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<td>18:00</td>
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Programe for Asian Congress 2016

<table>
<thead>
<tr>
<th>Session</th>
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<tbody>
<tr>
<td>1. Asian trends in 3Rs of animal experiments</td>
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<tr>
<td>2. Cosmetics regulation and alternatives in Animal Experiments</td>
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<tr>
<td>3. 3Rs in pesticides and Chemicals</td>
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<tr>
<td>4. 3Rs in Biologicals and others</td>
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<td>5. Future Approaches to alternatives in 3Rs</td>
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Plenary Lecture

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Affiliation</th>
<th>Country</th>
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<tbody>
<tr>
<td>Herman B.W.M. Koeter</td>
<td>Chairman of the Alternatives Congress Trust (ACT)</td>
<td>Italy</td>
</tr>
<tr>
<td>Troy Seidle</td>
<td>Humane Society International</td>
<td>USA</td>
</tr>
<tr>
<td>Joanne Zurlo</td>
<td>Center for Alternatives to Animal Testing (CAAT) and Johns Hopkins University</td>
<td>USA</td>
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</tbody>
</table>
Conclusion

According to International trend, I expect the development and validation of novel alternative to animal methods in China. I am sure China will join the ICCR, ICATM and OECD activities on the novel test methods for regulatory acceptance.
Policy and Mission: JaCVAM's policy and mission is to promote the 3Rs in animal experiments for the evaluation of chemical substance safety in Japan and establish guidelines for new alternative experimental methods through international collaboration.

the 3Rs in animal experiments—Reduction (of animal use)
Refinement (to lessen pain or distress and to enhance animal well-being)
Replacement (of an animal test with one that uses non-animal systems or phylo-genetically lower species)
(OECD GD34)