

## Workshop 7

# The Japanese Center for the Validation of Alternative Methods (JaCVAM): Recent Progress and Future Plans for the Validation and Acceptance of Alternative Testing in Japan



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# JaCVAM roles

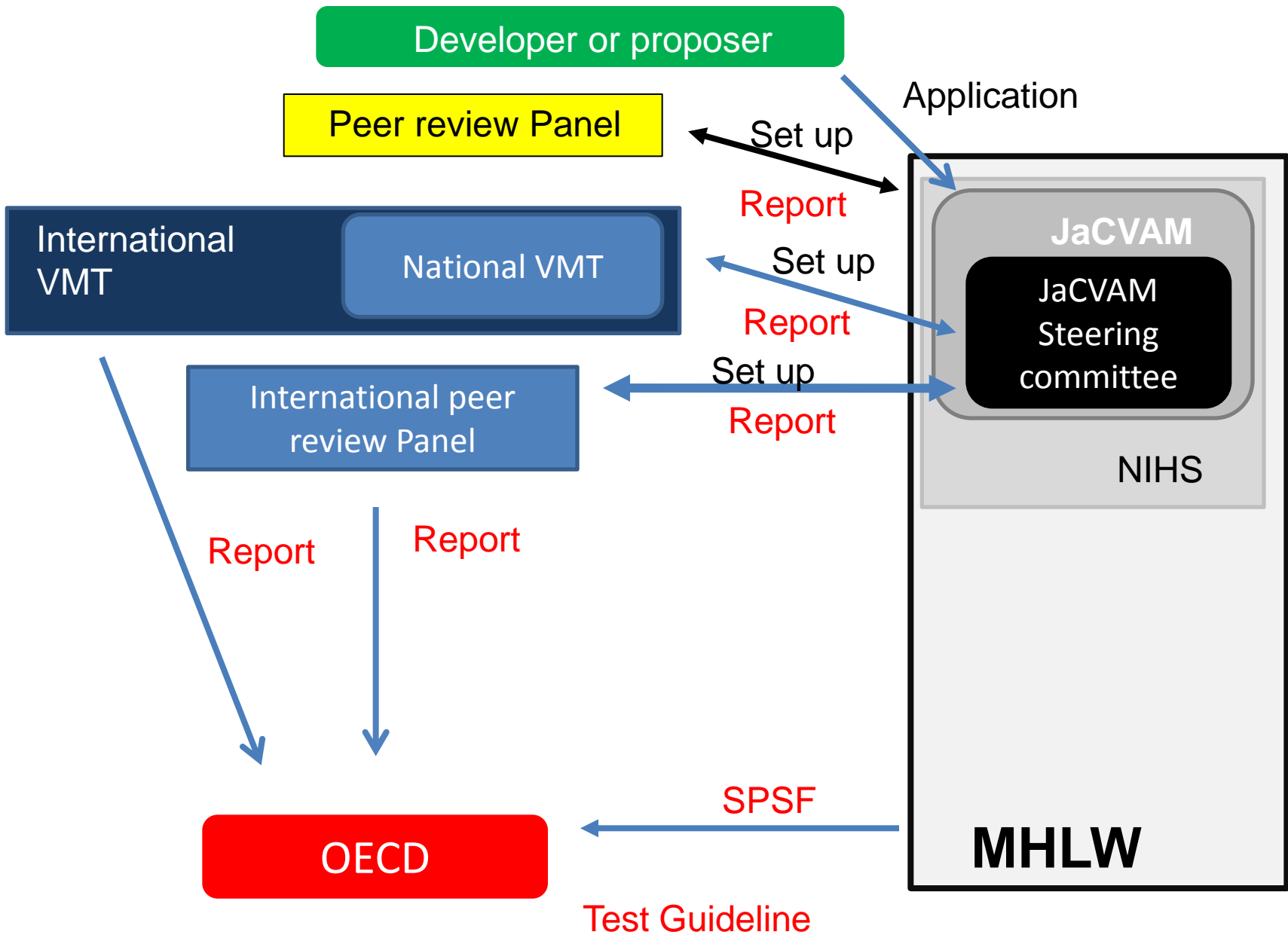
JaCVAM was established to promote the use of alternative methods to animal testing in regulatory studies, thereby replacing, reducing, or refining (the 3 Rs) the use of animals wherever possible while meeting the responsibility of the BSRC to ensure the protection of the general public by assessing the safety of chemicals and other materials, as stipulated in the regulations of the NIHS.

- 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 and other products** as well as to revisions to standards for cosmetic products.



**To establish guidelines for new  
alternative experimental methods  
through international collaboration**





**Japanese System for a new or revised test method**

# OECD Test Guidelines developed by Japanese

- ◆ Performance-Based Test Guideline for Stably Transfected Transactivation In Vitro Assays to Detect Estrogen Receptor Agonists No.455
- ◆ Skin sensitization assay, LLNA : DA No.442A
- ◆ Skin sensitization assay, LLNA : BrdU-ELISA No.442B
- ◆ Skin irritation assay with LabCyte EPI-MODEL 24

# Preparing Draft Test Guideline

- Bhas 42 cell transformation assay
- Short Time Exposure (STE) assay for eye irritation testing
- *in vivo* comet assay for genotoxicity testing

During the OECD WNT commenting round



# Japanese developed methods undergoing International peer review

- h-CLAT assay for skin sensitization testing  
(In preparation with EURL ECVAM)
- Short Time Exposure (STE) assay for eye irritation testing  
(On-going by ICCVAM)
- *in vivo* comet assay for genotoxicity testing  
(On-going by OECD expert)
- Reactive Oxygen Species (ROS) assay for phototoxicity testing  
(On-going by JaCVAM)

Supported by Dr. Kim Bae-Hwan (Keimyung University)



# JaCVAM on-going International validation studies

1. IL-8 reporter gene assay for skin sensitization testing

Supported by KoCVAM & Ai Young Lee

2. SIRC-CVS assay for eye irritation testing

Supported by KoCVAM & Biototeck

3. Stable transfected transcriptional activation (STTA) antagonist assay for endocrine disruptor screening

**Experimental part ended in March 2013**

Supported by NIFDS, Korea

4. Hand-1 Luc assay for reproductive assay

**First VMT meeting was held in Osaka, February, 2013**

Supported by KoCVAM & Eui-Bae Jeung, (Chungbuk National University)





# New validation studies in 2013

- Vitrigel-EIT for eye irritation assay (supported by MAFF)

First VMT meeting will be held in Tokyo,  
October, 2013 It will be supported by KoCVAM

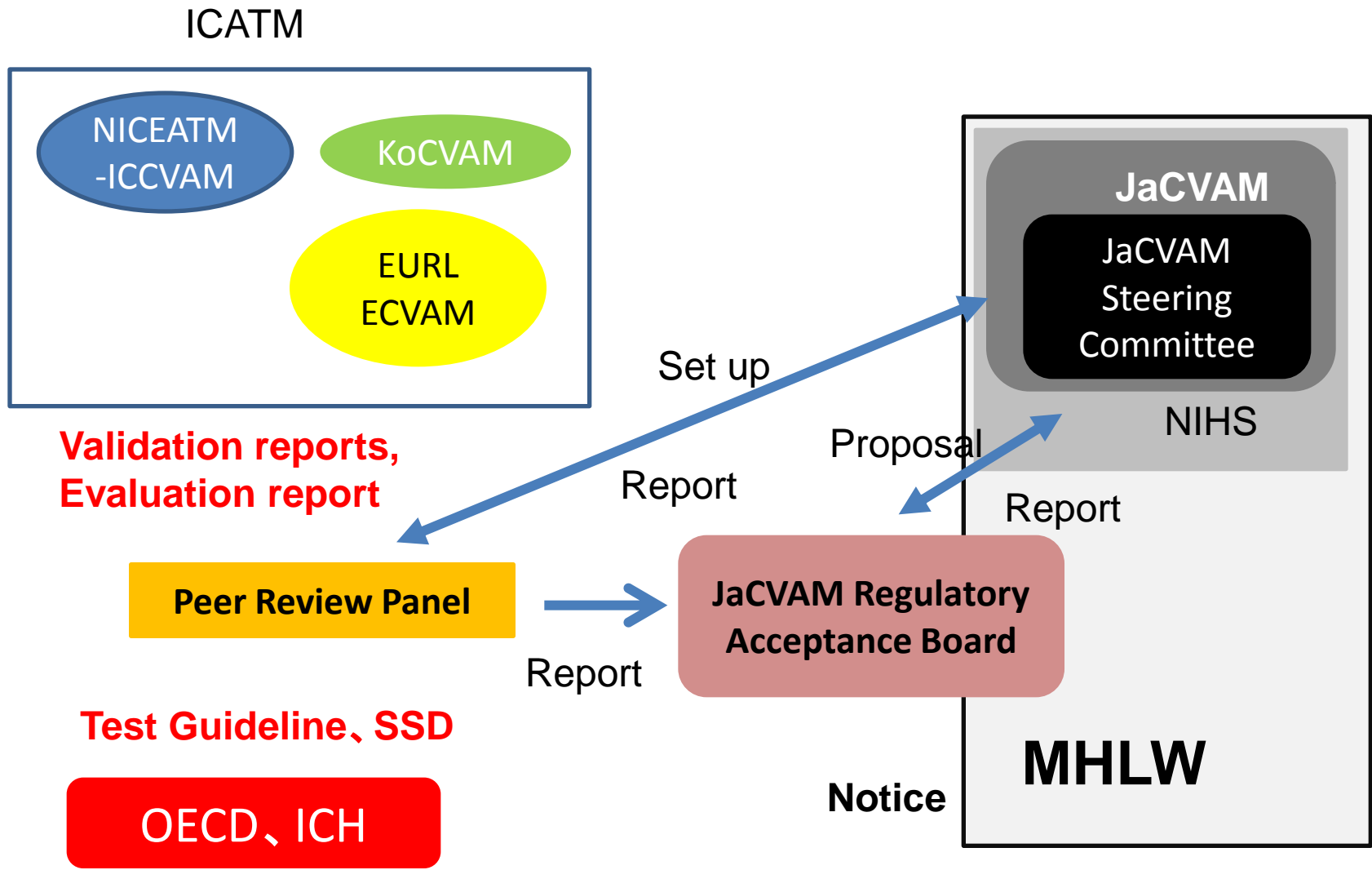
- Stable transfected transcriptional activation (STTA) assay for Androgen disruptor screening(AR-Ecoscreen) (supported by METI)

First VMT meeting will be held in Tokyo,  
September, 2013 It will be supported by NIFDS, Korea



Beneficial to application and approval  
for regulatory use





## Regulatory acceptance system in JaCVAM



# Accepted methods by the JaCVAM regulatory acceptance board by 2011

- ◆ The Bovine Corneal Opacity and Permeability (BCOP) Test Method for Identifying Ocular Corrosives and Severe Irritants
- ◆ The Isolated Chicken Eye (ICE) for Identifying Ocular Corrosives and Severe Irritants
- ◆ *In vitro* skin irritation testing: EPISKIN, EpiDerm, SkinEthics
- ◆ *n vitro* skin corrosion testing: Vitrolife-Skin, EpiDerm
- ◆ *In vitro* cytotoxicity test methods for estimating starting doses for acute oral systemic toxicity tests
- ◆ Skin sensitization assay, LLNA : DA
- ◆ Skin sensitization assay, LLNA : BrdU-ELISA
- ◆ Skin sensitization assay, rLLNA
- ◆ Eye irritation assay, Fluorescein Leakage assay

# On-going methods by the JaCVAM regulatory acceptance board

- Eye irritation testings Revised TG405, BCOP, ICE, CM
- Skin irritation LabCyte EPI-MODEL
- Skin penetration *in vitro* assay
- Skin sensitization DPRA, KeratinoSens
- Genotoxicity *in vitro* mammalian assay
- Cell transformation SHE assay, Bhas 42 assay
- Endocrine disrupter BG1 Luc ERTA



# Summary

- JaCVAM establishes test guidelines for new alternative experimental methods through international collaboration.
- JaCVAM encourages to conduct the application and approval of new alternative experimental methods for regulatory use.





About JaCVAM



Update on JaCVAM



Academic activities



Submission of Alternative  
Methods to JaCVAM



International Cooperation

# Thank you for your attention

**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)

## News

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