

SACATM meeting, September 6, 2012
NICEATM

The Japanese Center for the Validation of Alternative Methods (JaCVAM): update



Hajime Kojima, Akiyoshi Nishikawa -
JaCVAM, NIHS, Japan -

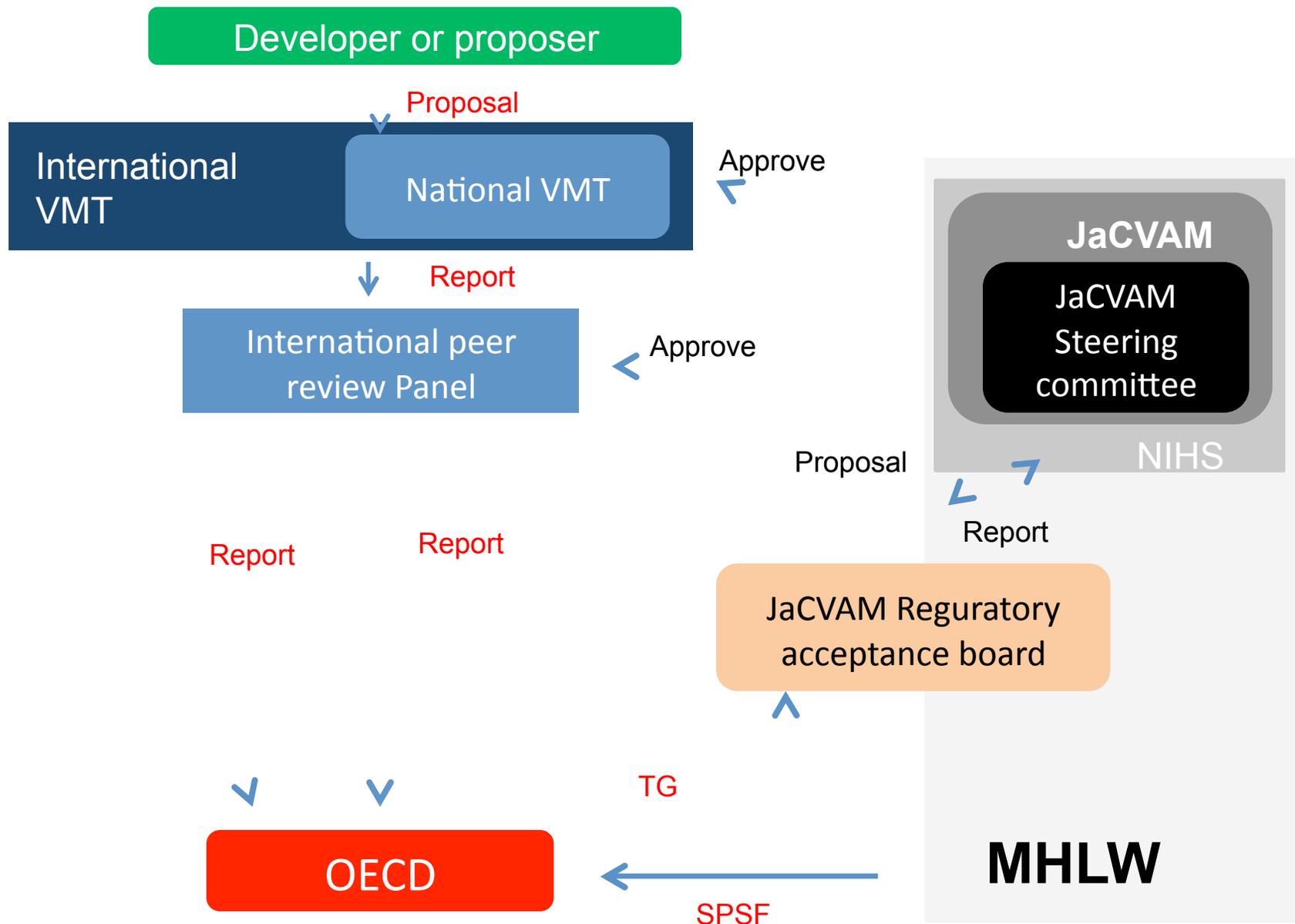
Contents

- JaCVAM roles to application and approval for the manufacture and sale of pharmaceutical and other products
- JaCVAM roles to cooperate and collaborate with similar organizations in related fields, both in Japan and internationally

Rules of Operation at the Japanese Center for the Validation of Alternative Methods

Article 2: **Roles and responsibilities of JaCVAM**

2-1. 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 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.**



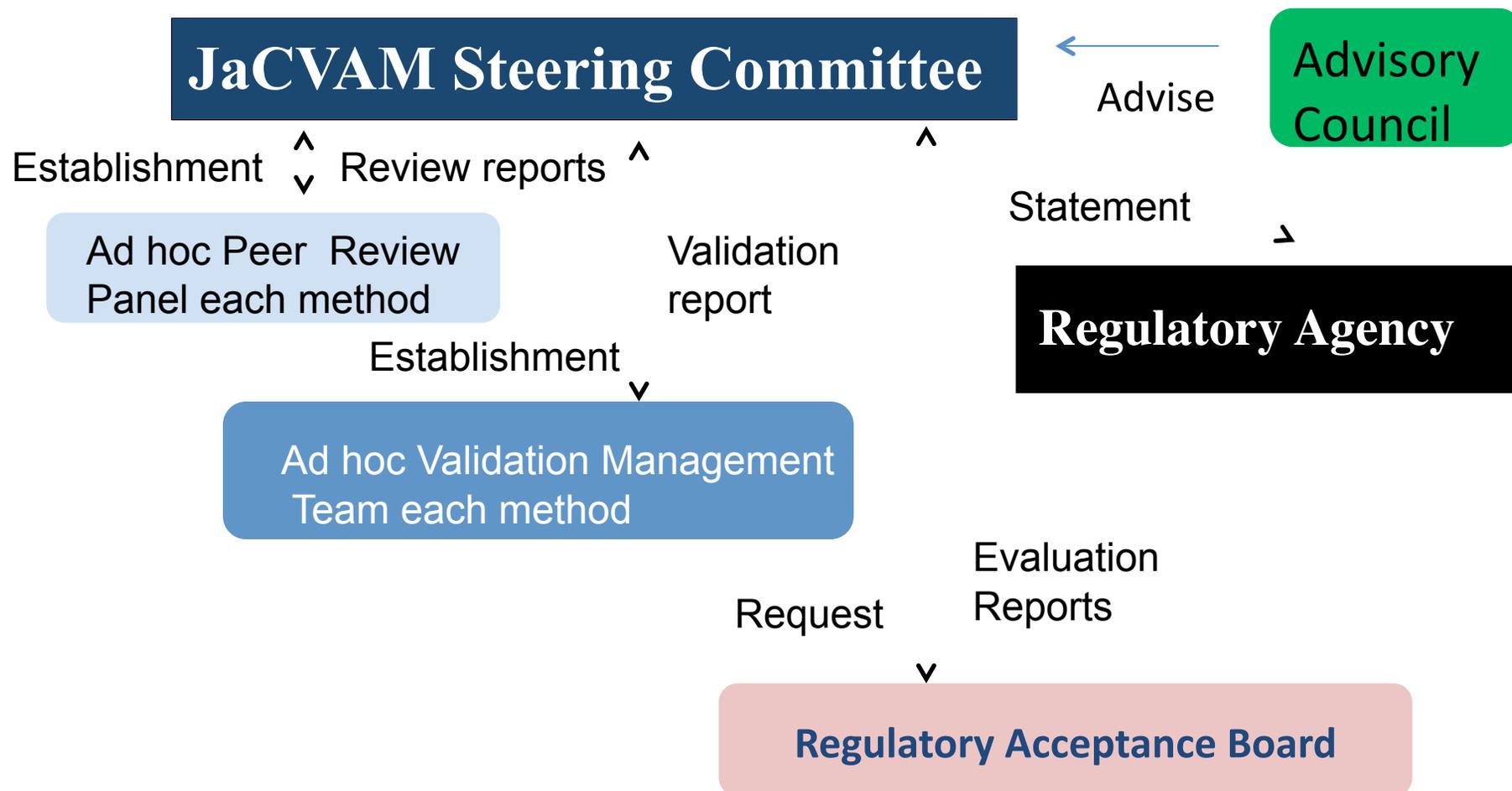
Japanese System for a new or revised test method

Rules of Operation at the Japanese Center for the Validation of Alternative Methods

Article 5: The Steering Committee

5-1. The Steering Committee deliberates on the selection of novel and modified methods for study by JaCVAM as well as finalizes budgetary and manpower allocations necessary to determine scientific validity and implement evaluation of the methods selected for study. It also deliberates on reports from the Regulatory Acceptance Board, establishes the official policy of JaCVAM regarding test methods judged to be suitable for regulatory studies, and issues documentation of the results of these activities, which are then submitted to relevant agencies at the Ministry of Health, Labour and Welfare (MHLW) as well as made available to the public.

Organization of JaCVAM since April, 2011



Administrative Notice for quasi-drug by MHLW in 2011

RE: JaCVAM activities to promote the use of test results obtained from alternatives to animal testing in applications for approval of quasi drugs

We invite you to make reference to information available on the JaCVAM Website (<http://jacvam.jp/>) in ensuring proper preparation of applications for approval of manufacturing and sales of quasi drugs as well as to requests for revisions to positive lists for cosmetics. We also kindly request that you publicize this information to applicable businesses and other concerned parties operating under your jurisdiction.

The JaCVAM Website is available at <http://jacvam.jp/>.

Accepted methods by the JaCVAM regulatory acceptance board in 2011 & 2012

- ◆ *In vitro* cytotoxicity test methods for estimating starting doses for acute oral systemic toxicity tests
- ◆ rLLNA for skin sensitization assay
- ◆ Epiderm and SkinEthics for skin irritation assay

On-going methods by the JaCVAM regulatory acceptance board in 2012

- Fluorescence Leakage test for eye irritation assay
- Cytosensor microphysiometer test for eye irritation assay
- Revised BCOP for eye irritation assay
- Revised TG 405: Eye irritation/Corrosion
- LabCyte EPI-MODEL 24 SIT for skin irritation assay
- In vitro skin absorption assay
- BG1 Luc assay for endocrine disruption screening
- In vitro mammalian assay for genotoxicity testings
- LLNA:DA and LLNA:BrdU-ELISA for skin sensitization assay

Administrative Notice for quasi-drug by MHLW in 2012

As part of its activities during 2011, a Regulatory Science Research program chaired by Dr. Hajime Kojima has prepared **guidance on the use of alternative methods to animal testing for skin-sensitization potency and phototoxicity in the safety assessment of quasi-drug and cosmetic products** and has made the guidelines available in order to promote the use of alternative methods. We kindly request that you publicize this information to concerned parties operating under your jurisdiction.

Rules of Operation at the Japanese Center for the Validation of Alternative Methods

Article 2: **Roles and responsibilities of JaCVAM**

2-2. 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.**

Accepted methods by the OECD Test Guideline in 2012, which is correlated with JaCVAM

- LabCyte EPI-MODEL 24 SIT for skin irritation assay
- BG1 Luc assay for endocrine disruption screening

On-going of International peer review

- Bhas cell transformation assay (with ECVAM)
- *In vivo* comet assay (with OECD)
- Short time exposure assay for eye irritation testing (**with NICEATM-ICCVAM**)
- ROS assay (with ICH S10)

History of Our Validation Effort (In Vivo comet assay)



▲ **1st** Start in Aug. At 5 lead labs with ethyl methanesulfonate (EMS)

2nd At 5 lead labs with EMS +3 coded chem.

3rd At 4 lead labs with EMS+3 coded chem.

4th (1st) At 13 labs with EMS+4 coded chem.

4th (2nd) At 14 labs with EMS+40 coded chem.

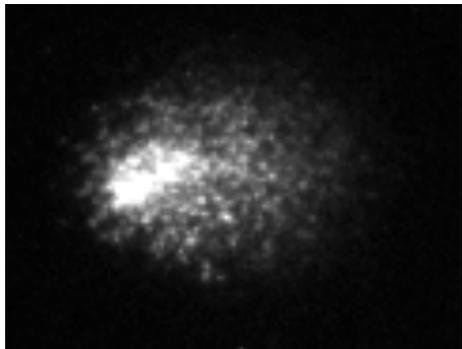
Protocol Optimization
Within/Between-Lab Variability

Optimized-Protocol Confirmation
Within/Between-Lab Variability

Lab Recruitment (Transferability)

Reproducibility

Predictive Capability



Request from OECD secretary

- In order to start working as soon as possible on **the Comet assay**, we will send a letter this week to the WNT requesting nomination for an expert group on the Comet assay. It will be necessary for this expert group to review the raw data from the labs that participated in the validation of the assay. So please send these data as soon as possible, even if the validation report is not finalized.

JaCVAM correlated on-going International - validation studies

1. h-CLAT assay for skin sensitization testing (**with ECVAM& ICATM**)
2. IL-8 reporter gene assay for skin sensitization testing (**with ICATM**)
3. Stable transfected transcriptional activation (STTA) antagonist assay for endocrine disruptor screening (with OECD VMG-NA)
4. SIRC-CVS cytotoxicity assay for eye irritation testing (**with ICATM**)

JaCVAM main work

- Under the ICATM framework, JaCVAM expects to experience more efficient test validation and review, as well as more rapid international acceptance of scientifically valid methods.
- To ensure that new or revised tests are validated through comparison with domestically developed or internationally certified standard tests, peer reviewed, and officially accepted by the regulatory agencies.

Update on JaCVAM website

- **【New】**
[We have updated “Regulations on the Foundation o JaCVAM” \(Aug.14,2012\)](#)
- **【New】**
[We have updated the Monthly Reports of JaCVAM Activities,Jul.2012 \(Aug.14,2012\)](#)
- **【New】**
[We have updated “The Regulatory Acceptance BoardReport” \(Aug.02,2012\)](#)
- **【New】**
[We have updated “Peer Review Panel Report” \(July.20,2012\)](#)
- **【Important】**
[We have updated "Administrative Notice, April 26,2012", \(May.17,2012\)](#)



Japanese Center for the Validation of Alternative Methods

Office : New Testing Method Assessment, Division of Pharmacology,
National Biological Safety Research Center (NBSRC),
National Institute of Health Sciences (NIHS)

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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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- 📧 news texts dummy texts news texts (2009.7.3)
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