

The International Cooperation on Alternative Test Methods
(ICATM): Translating Science to Provide Improved Public
Health Safety Assessment Tools

The Japanese Center for the Validation of
Alternative Methods (JaCVAM): Recent
ICATM contributions and Future plans



Hajime Kojima,
JaCVAM, NIHS, Japan



JaCVAM: Japanese Center for the Validation of Alternative Methods

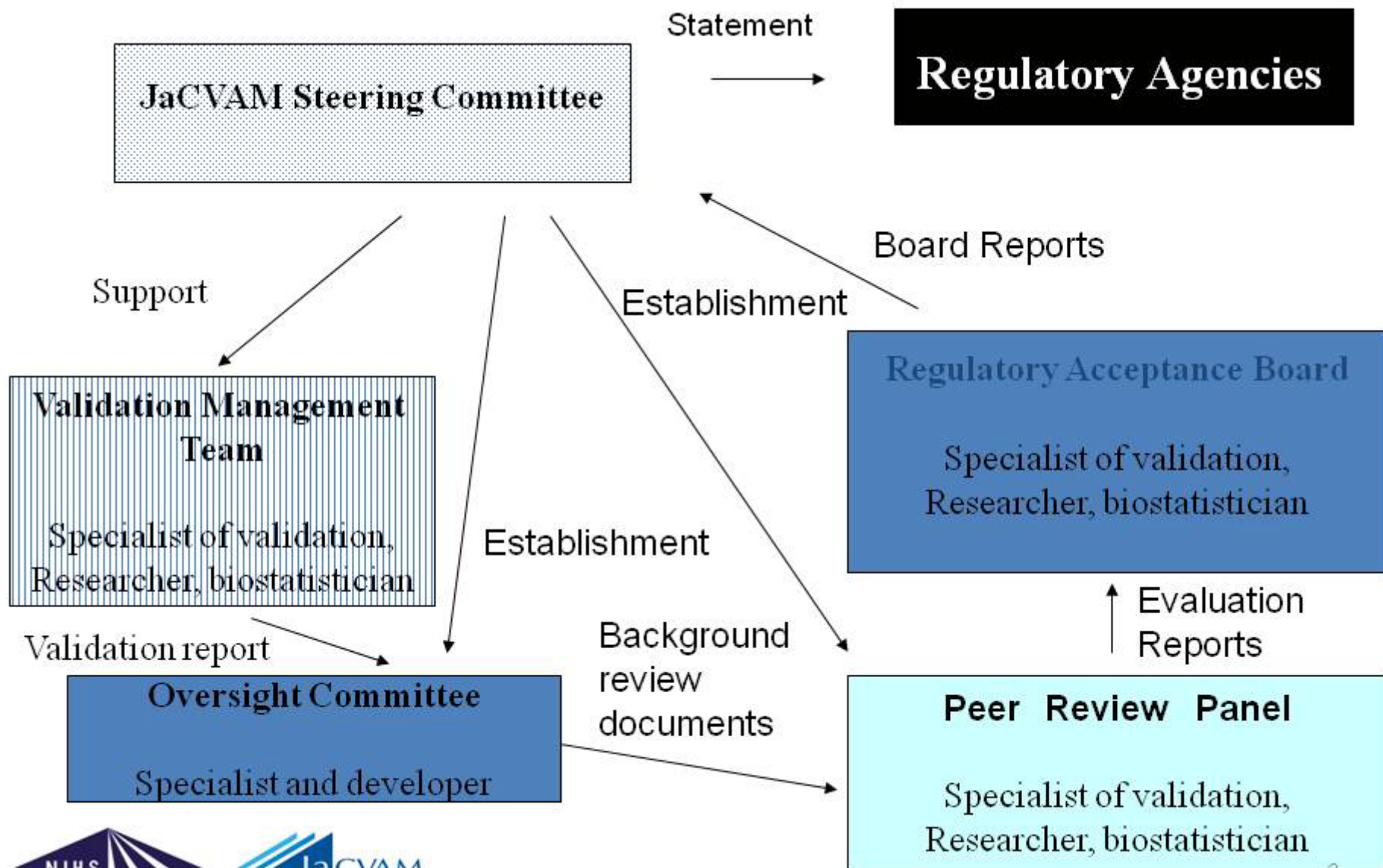
This center created at National Institute of Health Sciences (NIHS) in Japan, 2005. by the Ministry of Health, Labour and Welfare (MHLW).

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.



Framework for validation, peer review and regulatory acceptance of alternative methods



Accepted methods by the JaCVAM regulatory acceptance board

- ◆ 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
- ◆ Skin sensitization assay, LLNA:DA
- ◆ Skin sensitization assay, LLNA:BrdU-ELISA
- ◆ *In vitro* skin irritation testing: EPISKIN
- ◆ *In vitro* skin corrosion testing: Vitrolife-Skin, EpiDerm
- ◆ *In vitro* cytotoxicity test methods for estimating starting doses for acute oral systemic toxicity tests

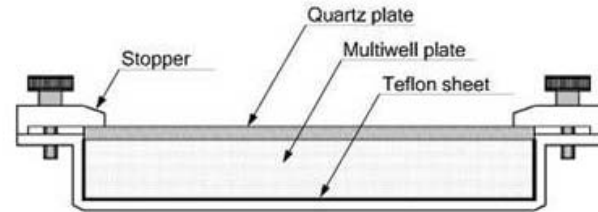
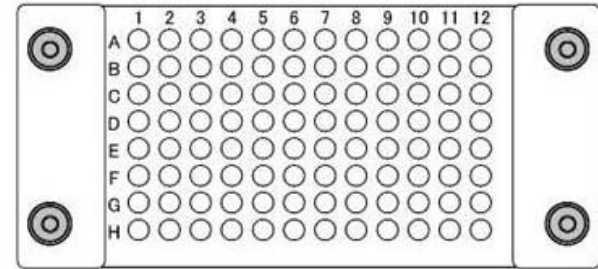
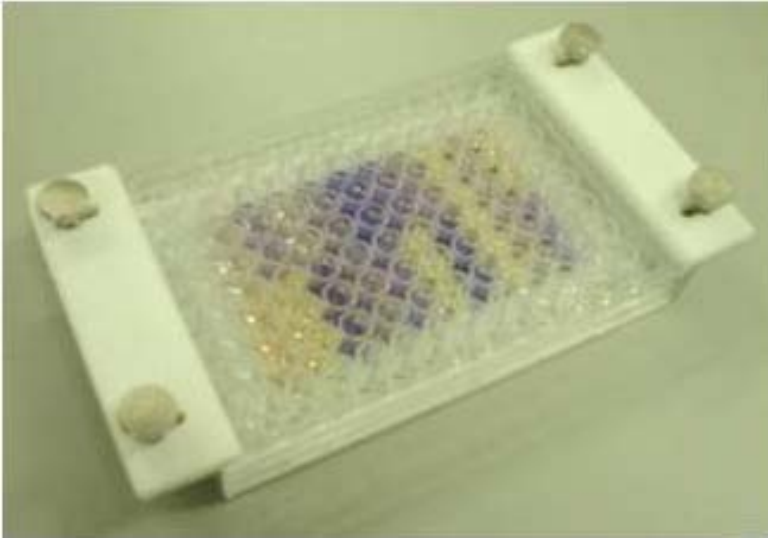
**To establish guidelines for new
alternative experimental methods
through international collaboration**



JaCVAM Organized Recent and On-going validation studies

- ◆ h-CLAT assay for skin sensitization testing
- ◆ *In vivo/in vitro* Comet assay for genotoxicity testing
- ◆ Stably Transfected Transcriptional Activation (STTA) antagonist assay for endocrine disruptor screening
- ◆ ROS assay for phototoxicity testing (in preparation)

High throughput ROS assay



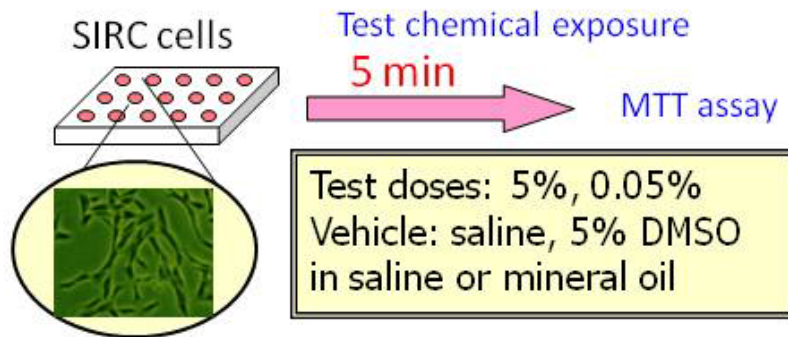
- Quartz reaction container for multiwell assay
- Solar simulator
 - Overnight assay (18 hr): LTX-01 (Xe lamp, 18 W/m²; Nagano Science)
 - Short-time assay (1 hr) : Suntest CPS (Xe lamp, 250 W/m²; Atlas)
- **Colorimetric determination of reactive oxygen species;**
 1. Singlet oxygen (¹O₂); bleaching of *p*-nitrosodimethylaniline (RNO)
 2. Superoxide (O₂⁻); reduction of Nitroblue tetrazolium (NBT)

Japanese developed methods undergoing National or International peer review

- SIRC assay for eye irritation testing
- MATREX assay for eye irritation testing
- LabCyte assay for skin irritation testing
- 3T3 cell transformation assay
- Bhas cell transformation assay
- Short time exposure assay for eye irritation testing

The Short Time Exposure (STE) test

3 x10³ of SIRC cells were plated into each well of a 96-well microplate and cultured in EMEM/FBS for 5 days (Or 6.0 x10³/well for 4 days). The test procedure afterwards is as follows.



$$\text{Cell Viability} = \frac{\text{test chemicals-treated (mean OD}_{570})}{\text{vehicle control (mean OD}_{570})} \times 100$$

Rank Classification

STE Score

5%	Score	0.05%	Score
70 < CV	0	70 < CV	1
70 ≥ CV	1	70 ≥ CV	2

CV: Cell viability



$$\text{5\% Score} + \text{0.05\% Score} = \text{STE Rank}$$

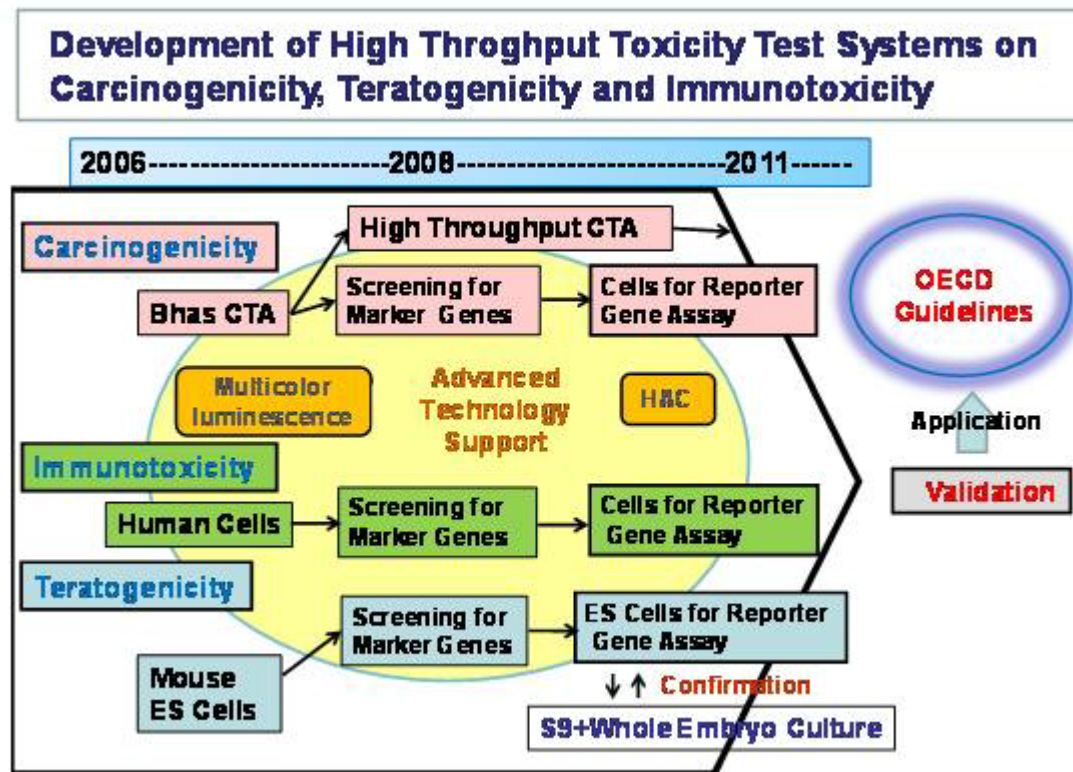
- 1 : Minimally irritating
- 2 : Moderately irritating
- 3 : Severely irritating

Category Classification

	Non Irritant (NI)	Irritant (I)
cell viability	> 70%	≤ 70%

Future plans

- Compellation on development of several alternative methods to Japanese colleague for hazard identification



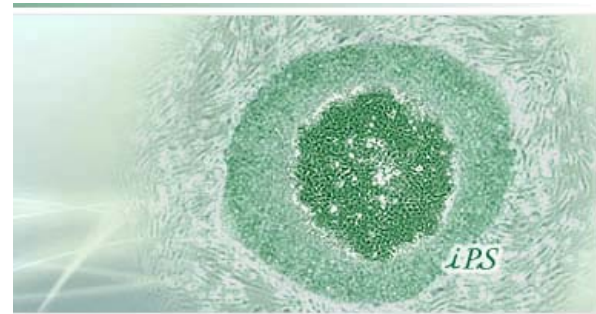
Long Term Future Plans

- alternative methods for long term toxicology testing
- alternative methods for risk assessment



Utilization of New technology

(-omics, pharmacokinetic (PK) modeling, new reporter gene cells, new materials, iPS and ES cells)



Thank you for your attention

JaCVAM - Windows Internet Explorer

http://www.our-net.co.jp/jacvamtest/en_index.html

Google

ファイル(F) 編集(E) 表示(V) お気に入り(A) ツール(T) ヘルプ(H)

お気に入り JaCVAM関連委員会 おすすめサイト Web スライス ギャラ...

JaCVAM

日本語 English Google Search WWW jaovam.jp

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)

About JaCVAM Update on JaCVAM Academic activities Submission of Alternative Methods to JaCVAM International Cooperation

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 Contents

ⓧ【NEW】news texts dummy texts news texts dummy texts news texts dummy texts(2009.7.16)

ⓧnews texts dummy texts news texts (2009.7.3)

ⓧnews texts dummy texts news texts dummy texts news texts dummy texts (2009.7.3)

ⓧAbout JaCVAM
Message from JaCVAM / Policy and Mission of JaCVAM / Organization of JaCVAM / Glossary / Proposal for Engagement Rules

ⓧJaCVAM Activities

インターネット | 保護モード: 有効 100%

3 エクスプローラ Corel Paint Sho... 2 Microsoft Of... nihs - Becky! JaCVAM - Windo... 12:18

