

JaCVAM **(the Japanese Centre for the** **Validation of Alternative Methods)** **Update**

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Today's Topics

- **International Validation studies on-going**
- **New Validation study in 2008**
- **Independent Scientific Peer Review and Recommendation to Regulatory Agencies**

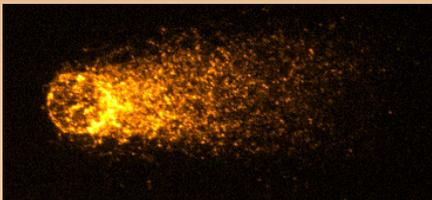


**International
Validation studies
On-going**



Steps of *in vivo* & *in vitro* Comet Validation Studies

	<u><i>in vivo</i></u>	<u><i>in vitro</i></u>
2006.8	Organized VMT	
2006.12	Start of Phase I	
2007.5	Start of Phase II	
2007.8		Organized VMT
2007.11		Start of Phase I
2008.1	Submission of SPSF to OECD	
2008.6	Start of Phase III	
2008.7		Start of Phase II
2009.4	Start of Phase IV (main)	Start of Phase III (main)

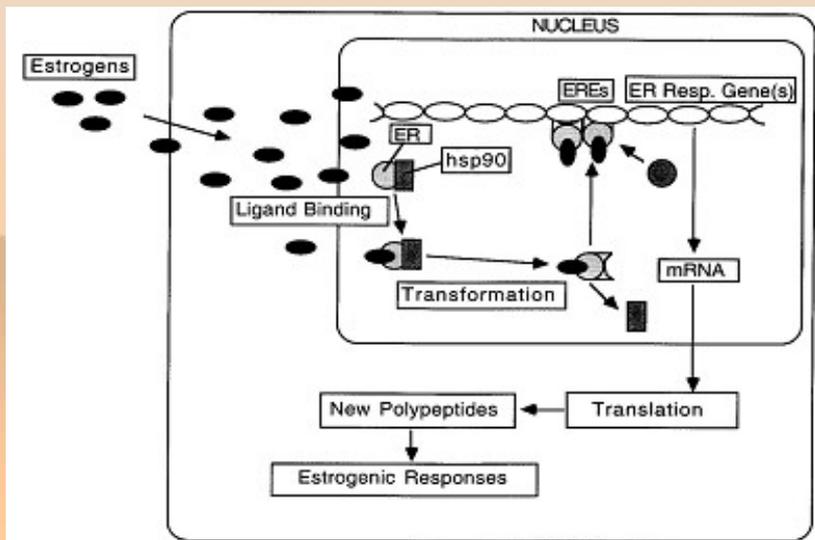


Information for the LUMI-CELL™ Estrogen Receptor Assay International Validation Effort

Leader : NICEATM

Labs: Each one lab. From USA, EU and Japan

Steps of this assay: Phase IIa study at Japanese Lab. is on-going. It is over on this June. Phase IIb will be started immediately. Japanese Lab. will participate until Phase III.



Follow up to the Peer Review of the Stably Transfected Transcriptional Activation (STTA) Assay and Technical Issues to be Addressed by the VMG NA 5

The PRP identified some areas where the eight validation criteria were not completely met and additional information should be provided. These included:

1. Criteria for positive responses were unclear and needs to be further elaborated;
2. Guidance on the criteria for acceptable test performance was insufficient, and,
3. The STTA assay can at this point only be used for estrogen agonist testing and **further studies would be needed if also estrogen antagonists could be tested.**

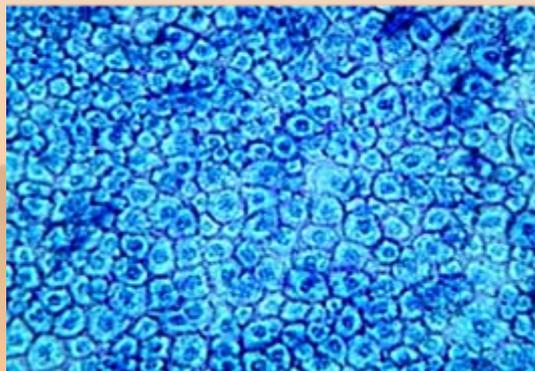
Current status: OECD draft test guideline

New Validation study in 2008

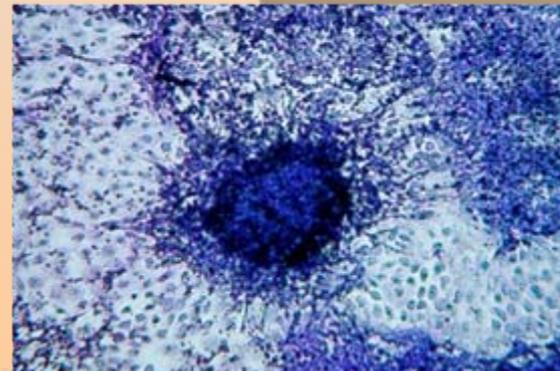


Cell Transformation Assay using Bhras cells

Type	Me-too test of SHE cells assay or Balb/c 3T3 assay
Developer	Food and Drug Safety Center in Japan
Coordinator	JaCVAM&ECVAM, NICEATM
Support	NEDO in Japan
Labs.	Three (International)
Start	January in 2009

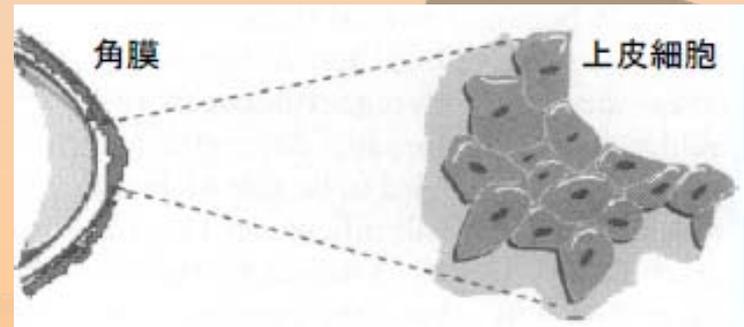


carcinogen



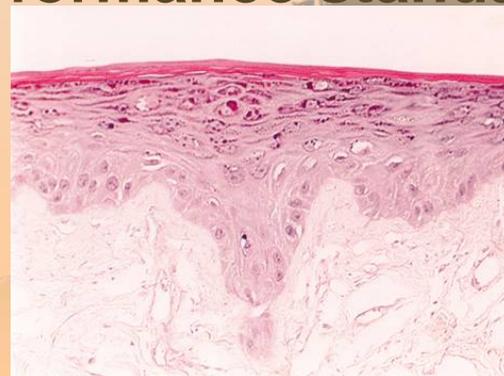
Validated 2008: Eye irritation

Method	Cytotoxicity test of Short Time Exposure (STE) assay using SIRC cells
Type	Formal
Developer	Kao in Japan
Coordinator	JSAAE (Japanese Society for Alternative to Animal Experiments)
Support Labs.	JaCVAM Five (only Japanese cosmetic companies)
Chemicals Start	25 (first step) June in 2008



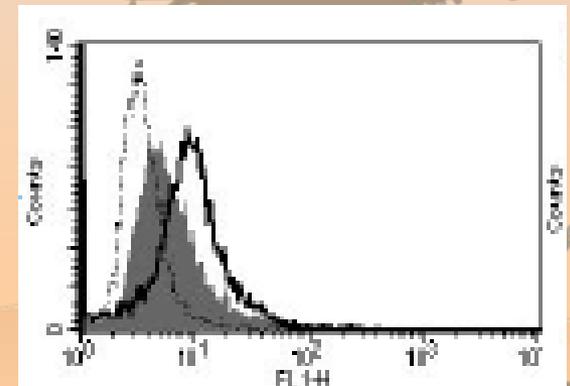
Validated 2008: Skin irritation

Method	EPISKIN method
Type	Me-too assay using Japanese 3-dimensional Epidermal model (LabCyte)
Developer	J-TEC
Coordinator	JSAAE (Japanese Society for Alternative to Animal Experiments)
Support Labs.	JaCVAM
Chemicals	Seven (only Japanese companies)
Start	19 (refer to ECVAM performance standard) June in 2008



Validated 2008: Skin sensitization

Method	h-CLAT using THP-1 cells
Type	Formal
Developer	Kao & Shiseido
Coordinator	ECVAM & JaCVAM
Support	ECVAM & MHLW
Labs.	Three (International)
Chemicals	Forty?
Start	2009



**Independent
Scientific
Peer Review
and
Recommendation
to Regulatory
Agencies**



Independent Scientific Peer Review

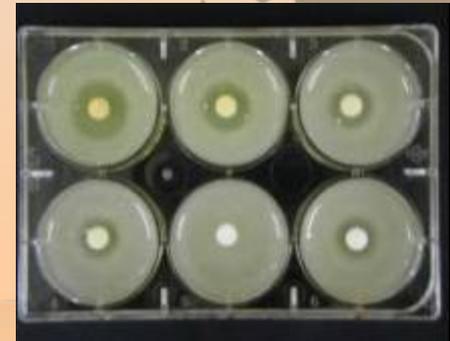
Cooperation to ICCVAM peer review

Immunotoxicity WG, Ocular Toxicity WG,
Dermal corrosive WG, Acute toxicity WG

These Japanese meetings will be started in a moment.

1. LLNA-BrdU (Japanese independent)

2. Battery system to predict phototoxicity: Yeast growth inhibition phototoxicity assay and red blood cell photohemolysis assay



Shadow Peer Review

These meetings are in progress.

Skin irritation EPISKIN

Ocular irritation BCOP and ICE

These meetings will be started in a moment.

Skin sensitization rLLNA

Pyrogen screening

Acute systemic toxicity

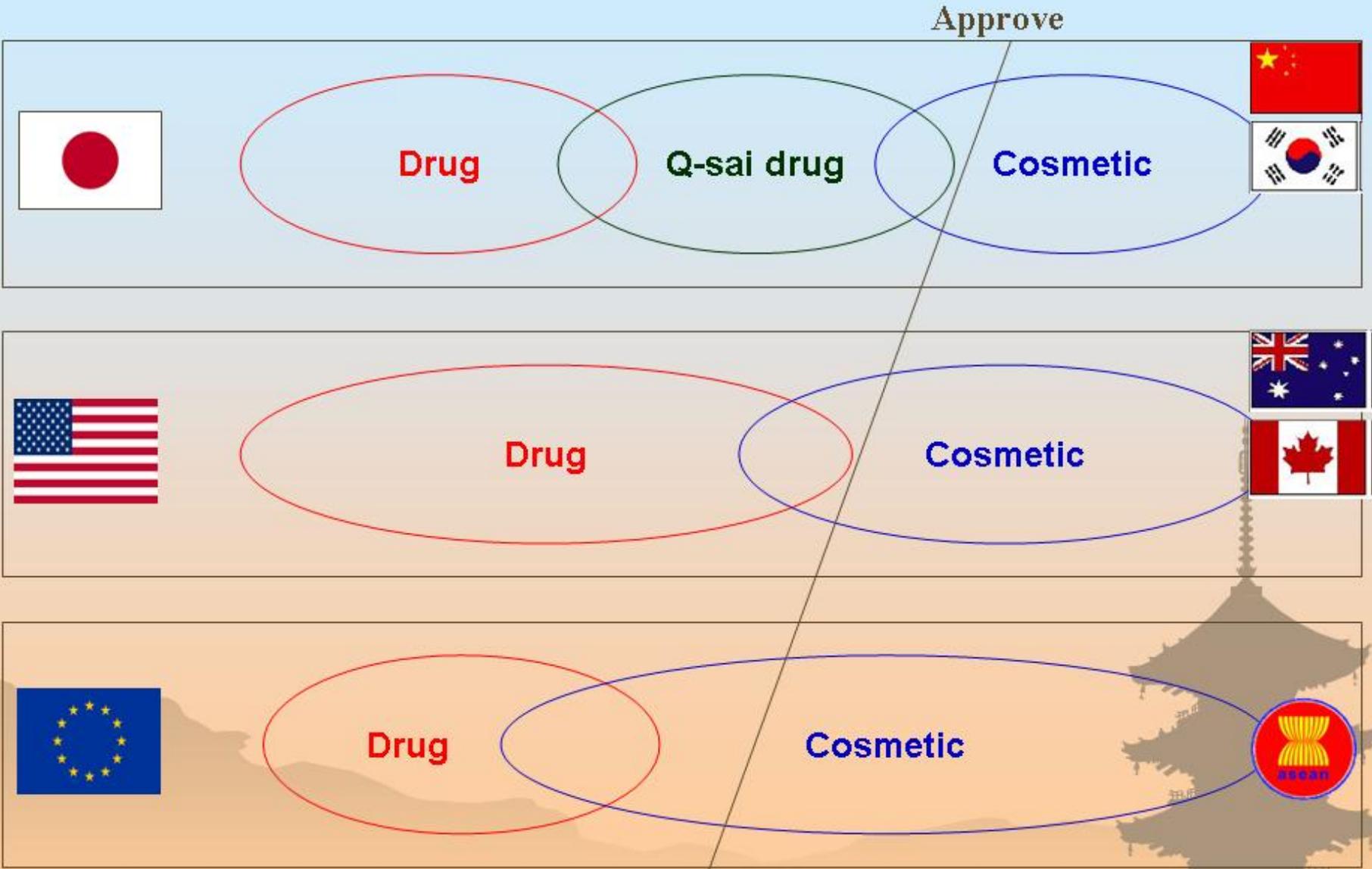


Regulatory acceptance

- Review of alternative to animal testing for safety evaluation of cosmetic ingredient using Qsai-drug
- Review of Japanese 3-dimensional human skin models for skin corrosivity tests
- Review of LLNA-DA
(Japanese independent organization)



Category classification of cosmetic and drug at each country





Prevent of breath or body odor	<ul style="list-style-type: none">• Body odor ⇒ OTC drug• Breath odor ⇒ Cosmetic	Cosmetic
Prevent of breast rash	OTC drug	Cosmetic
Hair growth or prevent of scurf, depilatory	<ul style="list-style-type: none">• Hair growth ⇒ OTC drug• Scurf ⇒ OTC drug• depilatory ⇒ Cosmetic	<ul style="list-style-type: none">• Cosmetic• Hair growth ⇒ each country law
Colorant	Cosmetic	Cosmetic
Permanent wave	Cosmetic	Cosmetic
Prevent of chalk mark, acne, sunburn	<ul style="list-style-type: none">• Chalk mark ⇒ Cosmetic• Acne, sunburn ⇒ OTC drug	Cosmetic
Disinfectant	OTC drug	Cosmetic
Bath	OTC drug	Cosmetic

Review of alternative to animal testing for safety evaluation of cosmetic ingredient using Qsai-drug

This organization has established in summer 2007.

Task Force

Regulatory
Acceptance
Board

Members:
JaCVAM, JCIA,
Dermatologists,
Regulator

Skin
irritation

Skin
Sensi-
tization

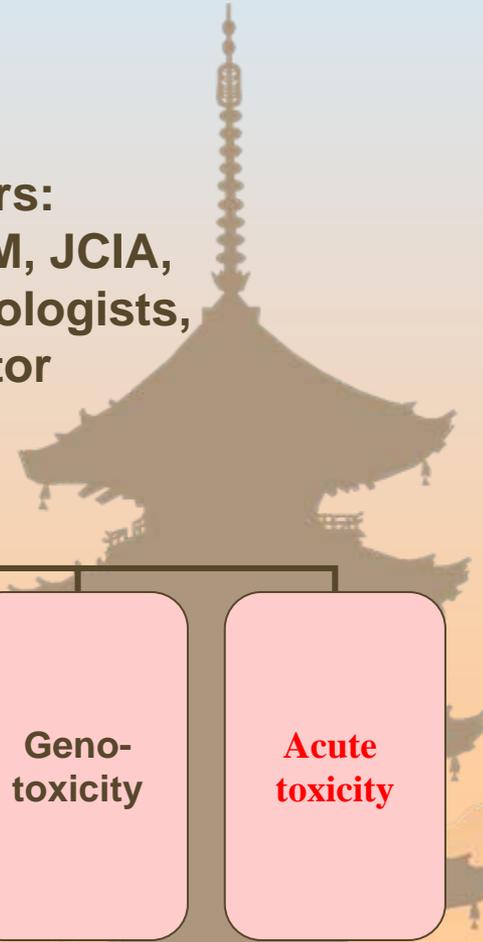
Skin
penetration
&
absorption

Eye
irritation

Photo-
toxicity

Geno-
toxicity

Acute
toxicity



ICCR & ICATM

JaCVAM demands to work together ICCR & ICATM as follows.

- **JaCVAM steering committee, regulatory acceptance board & advisory board**
- **Regulators of MHLW**
- **Japanese Cosmetic Industry Association**
- **Japanese Society for Alternative to Animal Experiments**



Thank you for your attention

