ICATM Activities

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Acting Director, NICEATM

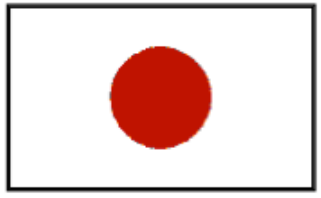
Acting Administrative Director, ICCVAM

Agency for Toxic Substances and Disease Registry • Consumer Product Safety Commission • Department of Agriculture
Department of Defense • Department of Energy • Department of the Interior • Department of Transportation
Environmental Protection Agency • Food and Drug Administration • National Institute for Occupational Safety and Health
National Institutes of Health • National Cancer Institute • National Institute of Environmental Health Sciences
National Library of Medicine • Occupational Safety and Health Administration

ICATM

- International Cooperation on Alternative Toxicological Methods
- Original ICATM Memorandum of Cooperation (MOC) agreement signed in 2009 by: US (ICCVAM), Europe (ECVAM), Japan (JaCVAM), and Canada (Health Canada).
- Expanded in 2011 to include Korea (KoCVAM)
- Brazil petitioned to join ICATM in 2013

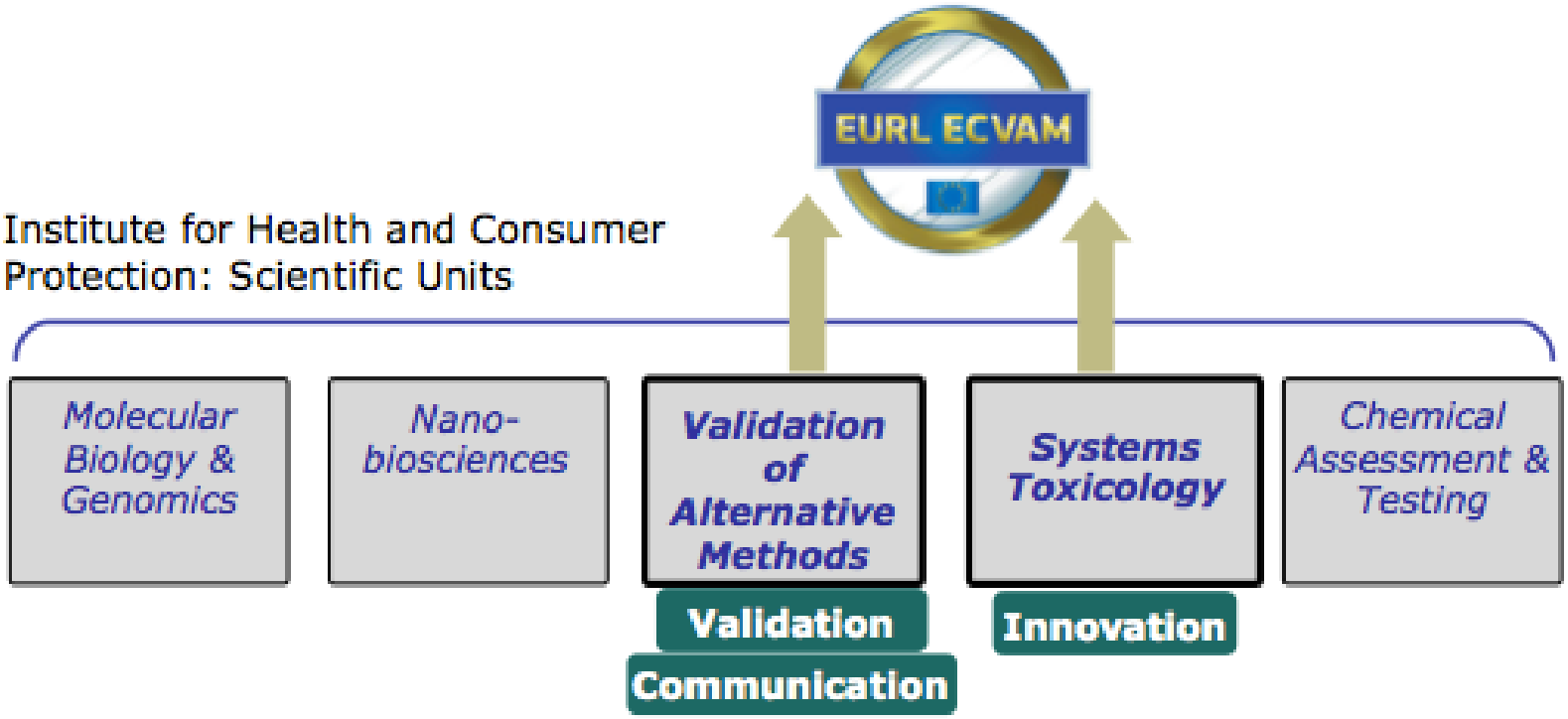


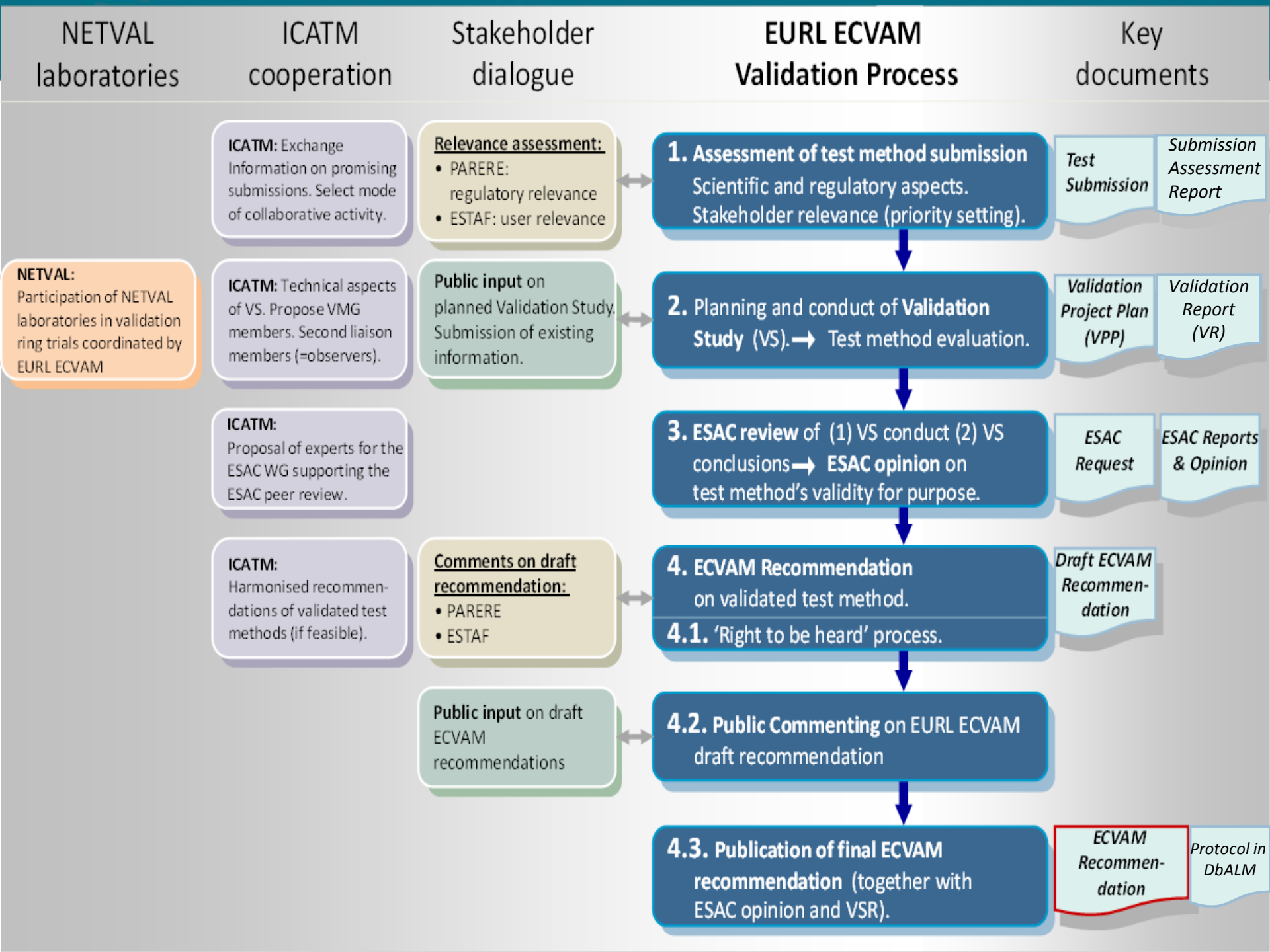

ICATM Goals

- Promote consistent and enhanced cooperation, collaboration, and communication among national validation organizations
- Incorporate transparency and stakeholder involvement
- Speed international adoption of valid alternative methods

EURL ECVAM


EURL ECVAM
Institute for Health and Consumer Protection: Scientific Units
Molecular Biology & Genomics
Nano-biosciences
Validation of Alternative Methods
Systems Toxicology
Chemical Assessment & Testing
Validation
Communication
Innovation

Validated Methods


NETVAL laboratories
ICATM cooperation
Stakeholder dialogue
EURL ECVAM Validation Process
Key documents
ICATM: Exchange Information on promising submissions. Select mode of collaborative activity.
Relevance assessment:
• PARERE: regulatory relevance
• ESTAF: user relevance
1. Assessment of test method submission
Scientific and regulatory aspects. Stakeholder relevance (priority setting).
Test Submission
Submission Assessment Report
NETVAL: Participation of NETVAL laboratories in validation ring trials coordinated by EURL ECVAM
ICATM: Technical aspects of VS. Propose VMG members. Second liaison members (=observers).
Public input on planned Validation Study. Submission of existing information.
2. Planning and conduct of Validation Study (VS). → Test method evaluation.
Validation Project Plan (VPP)
Validation Report (VR)
ICATM: Proposal of experts for the ESAC WG supporting the ESAC peer review.
3. ESAC review of (1) VS conduct (2) VS conclusions → ESAC opinion on test method's validity for purpose.
ESAC Request
ESAC Reports & Opinion
ICATM: Harmonised recommendations of validated test methods (if feasible).
Comments on draft recommendation:
• PARERE
• ESTAF
4. ECVAM Recommendation on validated test method.
4.1. 'Right to be heard' process.
Draft ECVAM Recommendation
Public input on draft ECVAM recommendations
4.2. Public Commenting on EURL ECVAM draft recommendation
4.3. Publication of final ECVAM recommendation (together with ESAC opinion and VSR).
ECVAM Recommendation
Protocol in DbALM

EURL ECVAM Priority Areas

- Skin sensitisation
- Endocrine Disruption
- Vaccine Safety Testing
- Carcinogenicity
- Toxicokinetics

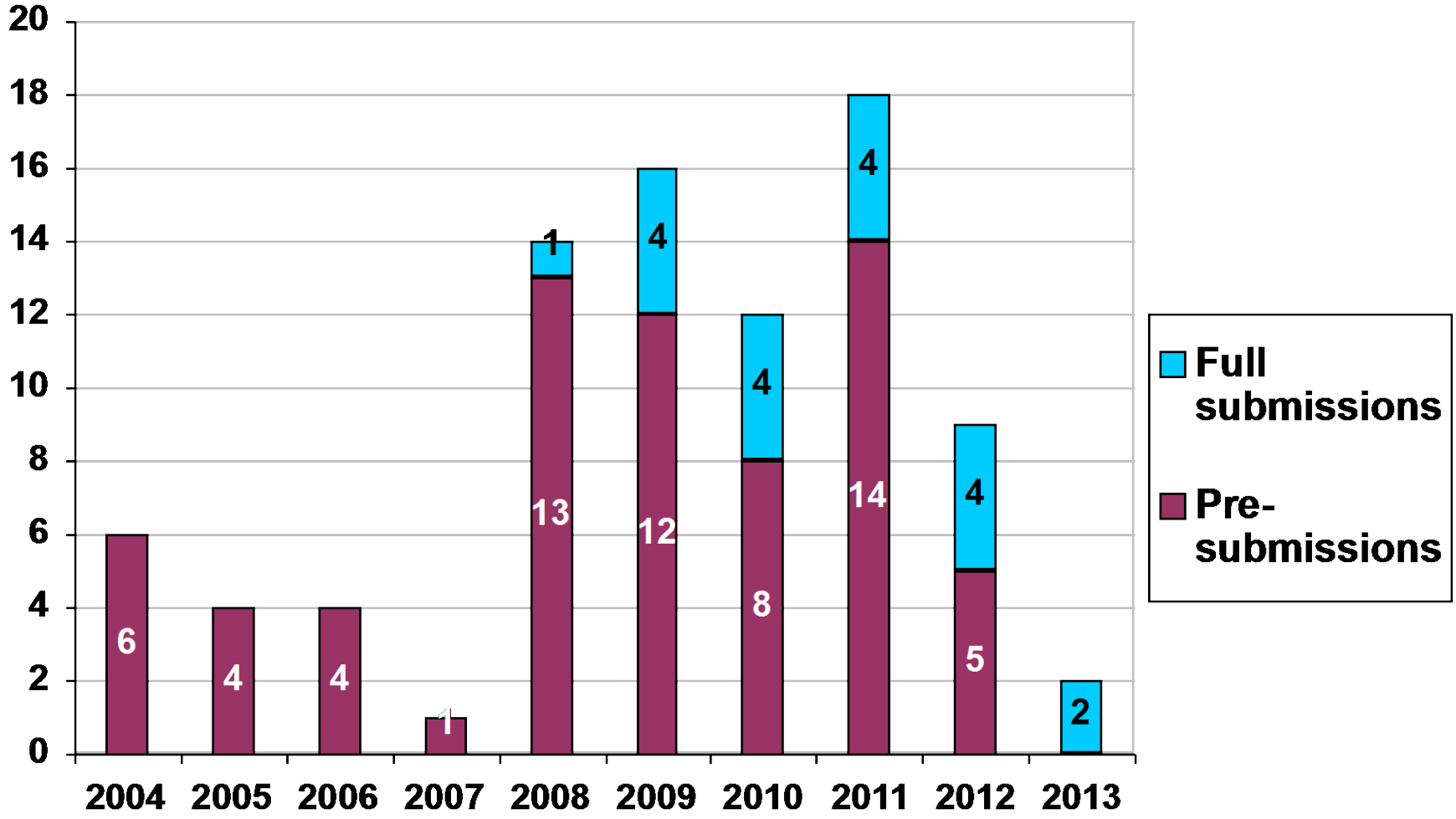
EURL ECVAM Priority Areas

- **Skin sensitisation**
- Endocrine Disruption
- Vaccine Safety Testing
- Carcinogenicity
- Toxicokinetics

EURL ECVAM Recommendations

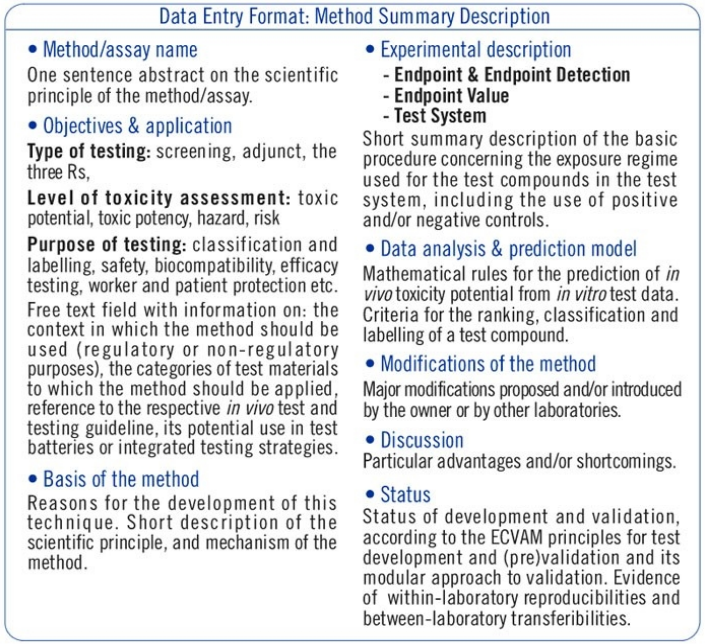
- **3T3 NRU** for identification of substances not requiring classification for acute oral toxicity published in April 2013
- Draft Recommendations on **DPRA** and **Bhas** sent to ICATM in May 2013
- Draft Recommendations expected by Q3 2013 for **KeratinoSens** (skin sen.) and **ZFET** (acute fish toxicity)

Test method submissions to EURL ECVAM since 2004



TSAR Database for Alt Methods

- **T**racking **S**ystem for **A**lternative methods towards **R**egulatory acceptance
- Tracking systems of all methods submitted to ECVAM for validation indicating the step within the overall process



Data Entry Format: Method Summary Description

- Method/assay name

One sentence abstract on the scientific principle of the method/assay.

- Objectives & application

Type of testing: screening, adjunct, the three Rs,

Level of toxicity assessment: toxic potential, toxic potency, hazard, risk

Purpose of testing: classification and labelling, safety, biocompatibility, efficacy testing, worker and patient protection etc.

Free text field with information on: the context in which the method should be used (regulatory or non-regulatory purposes), the categories of test materials to which the method should be applied, reference to the respective *in vivo* test and testing guideline, its potential use in test batteries or integrated testing strategies.

- Basis of the method

Reasons for the development of this technique. Short description of the scientific principle, and mechanism of the method.

- Experimental description
  - **Endpoint & Endpoint Detection**
  - **Endpoint Value**
  - **Test System**

Short summary description of the basic procedure concerning the exposure regime used for the test compounds in the test system, including the use of positive and/or negative controls.

- Data analysis & prediction model

Mathematical rules for the prediction of *in vivo* toxicity potential from *in vitro* test data. Criteria for the ranking, classification and labelling of a test compound.

- Modifications of the method

Major modifications proposed and/or introduced by the owner or by other laboratories.

- Discussion

Particular advantages and/or shortcomings.

- Status

Status of development and validation, according to the ECVAM principles for test development and (pre)validation and its modular approach to validation. Evidence of within-laboratory reproducibilities and between-laboratory transferibilities.

Seurat-1 Research Initiative

- Towards the replacement of *in vivo* repeat dose systemic toxicity testing
- Joint funding by the European Commission and a specific industrial sector (cosmetics industry / Colipa)

- SCR&Tox, "Stem Cells for Relevant Efficient Extended and Normalized Toxicology"
- HeMiBio, "Hepatic Microfluidic Bioreactor"
- DETECTIVE, "Detection of endpoints and biomarkers of repeated dose toxicity using in vitro systems"
- COSMOS, "Integrated In Silico Models for the Prediction of Human Repeated Dose Toxicity of COSMetics to Optimise Safety"
- NOTOX, "Predicting long-term toxic effects using computer models based onsystems characterization of organotypic cultures "
- ToxBank, "Supporting Integrated Data Analysis and Servicing of Alternative Testing Methods in Toxicology"

KoCVAM
NATIONAL INSTITUTE OF FOOD AND DRUG SAFETY EVALUATION

- MFDS launched the Korean research initiative on safety assessment of cosmetics (Funding: $ 3 million)

- Research fields
  - **Eye irritation**, Oral mucosal irritation, Skin sensitization, Photosensitization, *In silico* method, Standardization and validation

JaCVAM

- Created at National Institute of Health Sciences (NIHS) in Japan, 2005, by the Ministry of Health, Labour and Welfare (MHLW)

- Upcoming Peer Reviews:
  - ROS assay for photoxicity testing (Aug 2013)
  - h-CLAT assay for skin sensitization testing (w/ EURL ECVAM)

Questions?