



Interagency Coordinating Committee on the Validation of Alternative Methods

Updated ICCVAM Goals for FY2015

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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

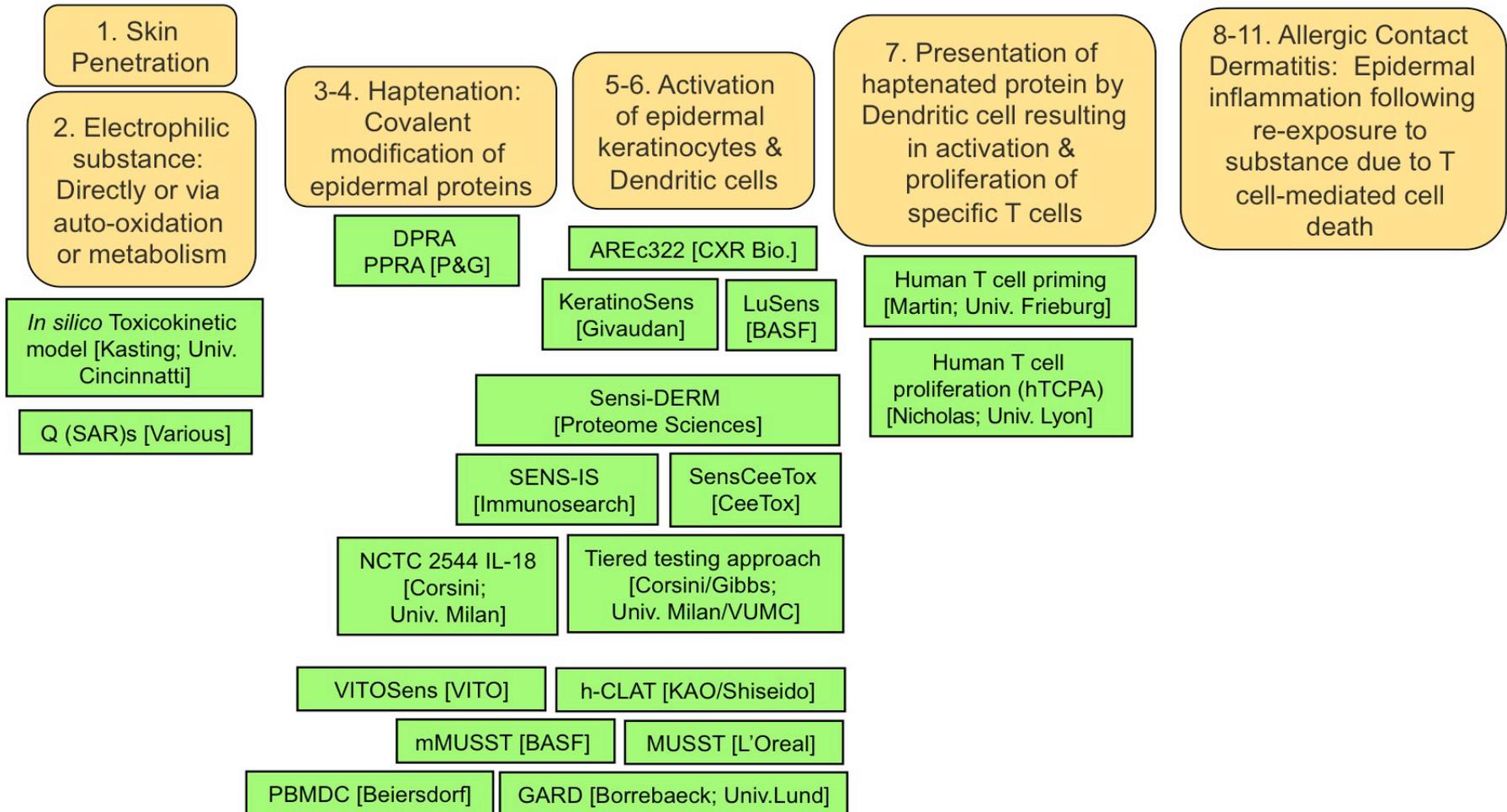
Priority Area: Acute Toxicity Testing

- FY 2015 Goals:
 - Finalize statistical analysis of the relative contribution of data from acute oral and dermal toxicity tests to pesticide hazard classification and labelling
 - Initiate projects related to reducing use of laboratory animal testing for the assessment of acute inhalation toxicity
 - Assist federal agency efforts to implement alternative assays related to eye irritation, skin irritation, and skin corrosion

Priority Areas: Skin Sensitization

- Fostering the evaluation and promotion of alternative test methods for skin sensitization has been one of ICCVAM's long-standing priorities.
- Promise for the near-term development of testing strategies that do not require the use of animals:
 - AOP for skin sensitization is well characterized
 - Number of non-animal test methods have been developed.
- FY 2015 Goals:
 - Continue providing expertise in the design and examination of the predictive value of a battery of *in vitro* and *in silico* methods
 - Evaluate a variety of approach(es) for integrating data from available non-animal methods to use in a prospective evaluation

Non-animal Methods for Skin Sensitisation: Aligned to AOP Key Events



Slide courtesy of Gavin Maxwell (Unilever/Cosmetics Europe)

Chemical Database

- DPRA, KeratinoSens, and h-CLAT data for 120 chemicals from published sources
 - Performed read-across predictions of sensitizer/nonsensitizer outcomes using OECD QSAR Toolbox
 - Collected physicochemical property data
 - Molecular weight
 - Octanol:water partition coefficient
 - Vapor pressure
 - Water solubility
 - Melting Point
 - Boiling Point

Skin Sensitization

- Machine learning: Artificial Neural Network (ANN), Bayesian Network (BN), Classification and Regression Tree (CART), Linear Discriminant Analysis (LDA), Logistic Regression (LR), Support Vector Machines (SVM)
- “Decision tree” approach
- Analysis submitted to OECD as an IATA case study skin sensitization & peer review manuscript in development.

Example Model: Skin Sensitization

SVM with h-CLAT + OECD + 6 PhysChem Properties

		LLNA		LLNA	
		NEG	POS	NEG	POS
Model	NEG	25	2	7	1
	POS	1	66	0	18
		Training set		Test set	

Specificity %:	96.2	100
Sensitivity %:	97.1	94.7
Accuracy %:	96.8	96.2

- Conclusion: machine learning models are superior to individual assay methods or battery, and achieve better balance between sensitivity and specificity.

Priority Area: Alternatives to HIST Vaccines

- FY 2015 Goal:
 - International working group on implementing *in vitro* assays as alternatives to the murine histamine sensitization test (HIST) for the testing of acellular pertussis vaccines

Communications Plans

- FY 2015 Goals:
 - Convened a Communities of Practice webinar in January, 2015
 - Developing reverse toxicokinetic models to correlate *in vitro* and *in vivo* activity
 - Convene an ICCVAM Public Forum (today)
 - Serve as a forum for communicating an agency position on test method recommendations
 - Serve as a forum for communicating how agencies are implementing the 3Rs
 - Update ICCVAM committee operating procedures and communicate them to stakeholders (completed)