



Interagency Coordinating Committee on the Validation of Alternative Methods

Update on NICEATM Activities

Warren M. Casey, Ph.D., D.A.B.T

Director, NICEATM

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



15 Years Out: Reinventing ICCVAM

February 1, 2013 Editorials Comments Off

Linda S. Birnbaum

Director, NIEHS and NTP, National Institutes of Health, Department of Health and Human Services, Research Triangle Park, North



Linda S. Birnbaum

“Toxicology testing is shifting from a primary focus on adverse phenotypic observations in animals to mechanism-based biological outcomes in vitro, and the NIEHS is embracing this paradigm shift through its participation in the multiagency Tox21 consortium (Collins et al. 2008). NICEATM will expand its scope and concentrate its resources on providing bioinformatic and computational toxicology support to NIEHS Tox21 projects.”

NICEATM

NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), organized as an office under the NTP Division, part of NIEHS



Alternative Models

NIH National Institute of Environmental Health Sciences



**Collaborative Workshop on Aquatic Models
and 21st Century Toxicology**

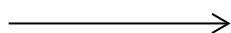
May 5-6, 2014
James B. Hunt Jr. Library
North Carolina State University
Raleigh, North Carolina, USA

Validation Models for Tox21

- Manual to HTS (BG1 ER TA)
- HTS only (validated data set)
- HTS to Manual

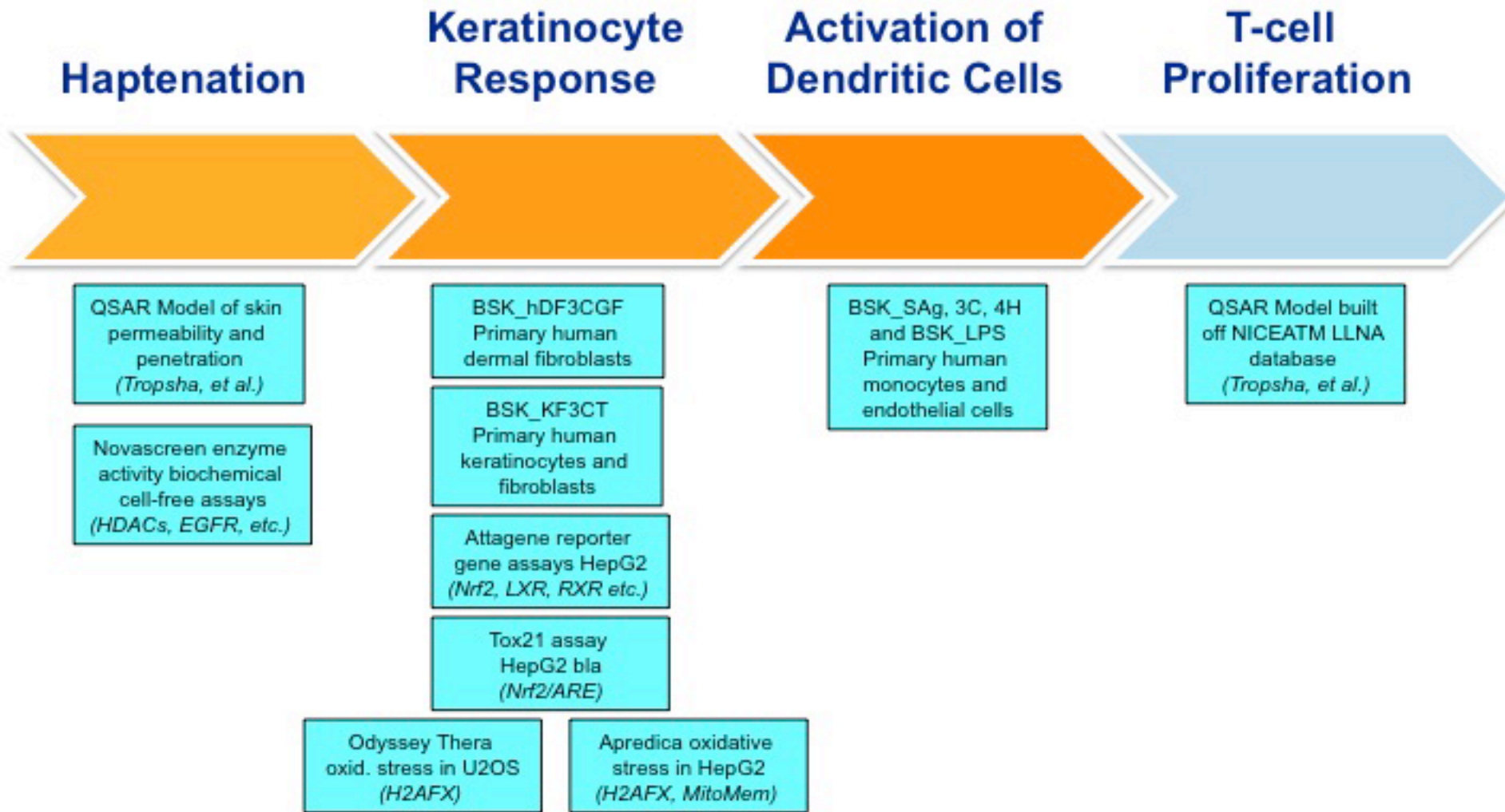


96-well (hand pipette)

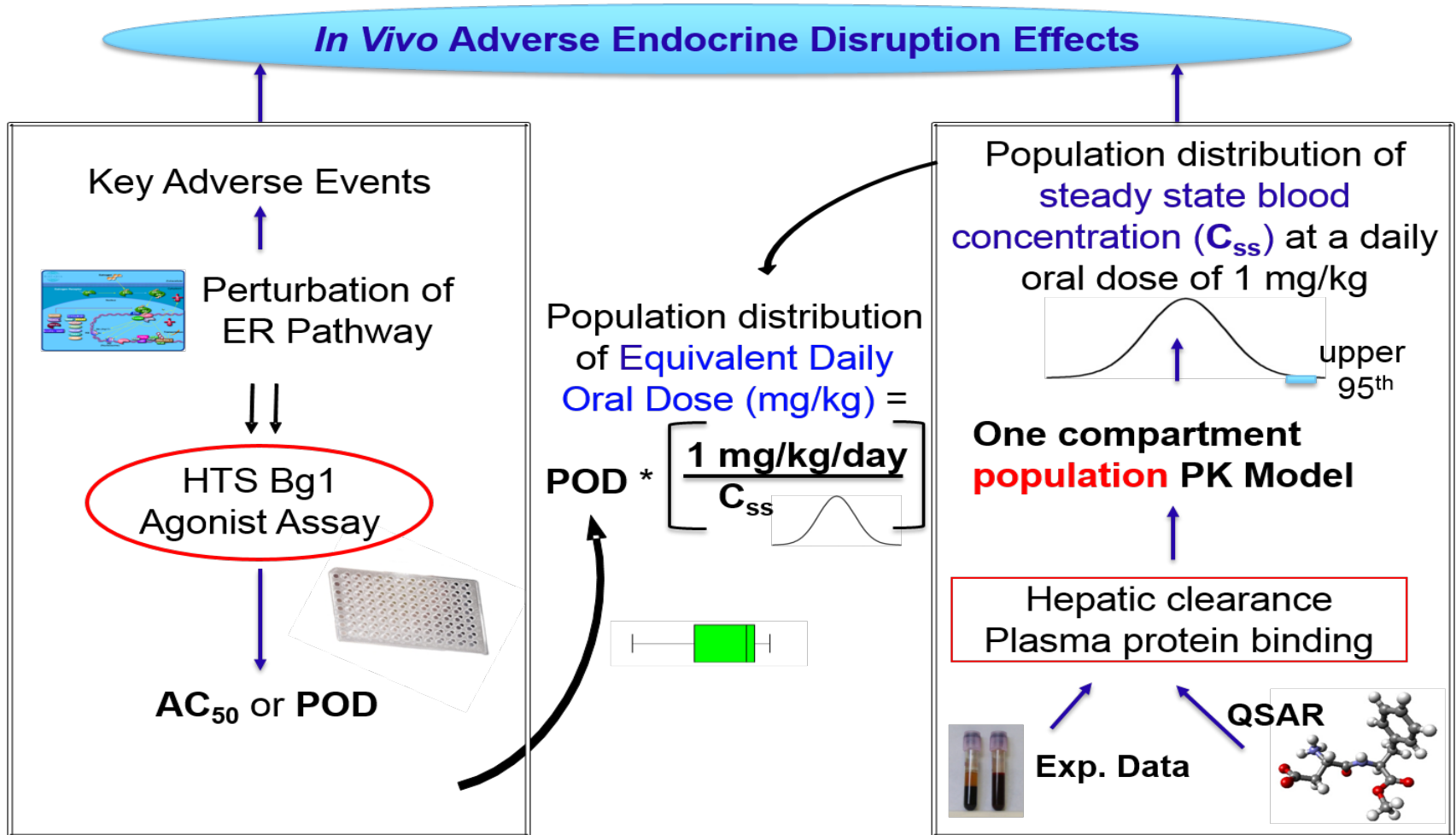


1536-well (fully automated)

ToxCast/Tox21 Data Analysis



In Vitro In Vivo Extrapolation (IVIVE)



In Vitro / In Silico Xenobiotic Metabolism Approaches

- Identify Practicable Approaches
- Assess Predictivity of Approaches
- Identify Subset(s) of Chemicals to Study in Metabolically Competent Systems



Substrate Predictions

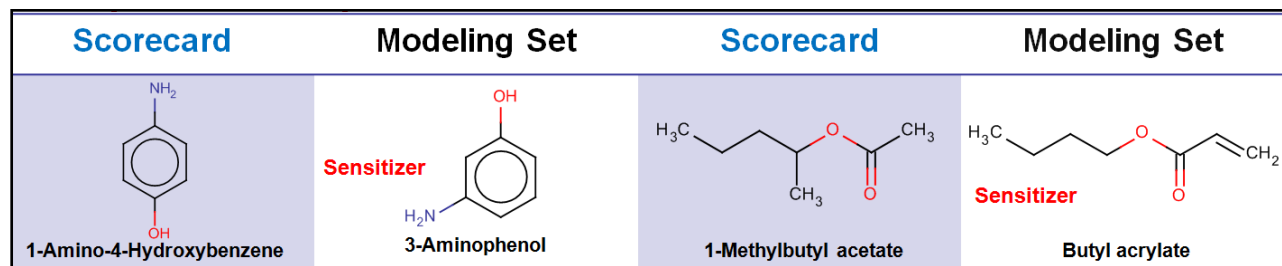
Metabolite Structure Predictions

Extent of Metabolism Predictions

Toxicity Module

QSAR Models

- A134 sensitizers and 128 non-sensitizers
 - Consensus model (75% coverage): 80% BA (5-fold cross val.)
- External validation on Scorecard dataset using QSAR models and similarity search
- Benchmarking with OECD QSAR Toolbox on 153 external compounds



	Sensitivity	Specificity	Coverage
Consensus	73%	91%	84%
OECD Toolbox	69%	20%	97%

Integrated Testing and Decision Strategies (ITDS)

*ALTEX Online first
published March 31, 2014
<http://dx.doi.org/10.14573/altex.1310151>*

SHORT COMMUNICATION

Open Source Software Implementation of an Integrated Testing Strategy for Skin Sensitization Potency Based on a Bayesian Network

Jason R. Pirone¹, Marjolein Smith¹, Nicole C. Kleinstreuer², Thomas A. Burns², Judy Strickland², Yuri Dancik⁴, Richard Morris¹, Lori A. Rinckel², Warren Casey³, and Joanna S. Jaworska⁴

¹Social and Scientific Systems, Inc., Durham, NC, USA; ²Integrated Laboratory Systems, Morrisville, NC, USA;

³National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods, Division of the National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA;

⁴Procter & Gamble NV, Strombeek-Bever, Belgium

High Quality Reference Data

Literature Searches “Uterotrophic”

- PubMatrix (keyword searches)
- FDA EDKB, other resources

Lit Review: >1200

Data Extraction

- Standardized ontology
- Local PDF repository

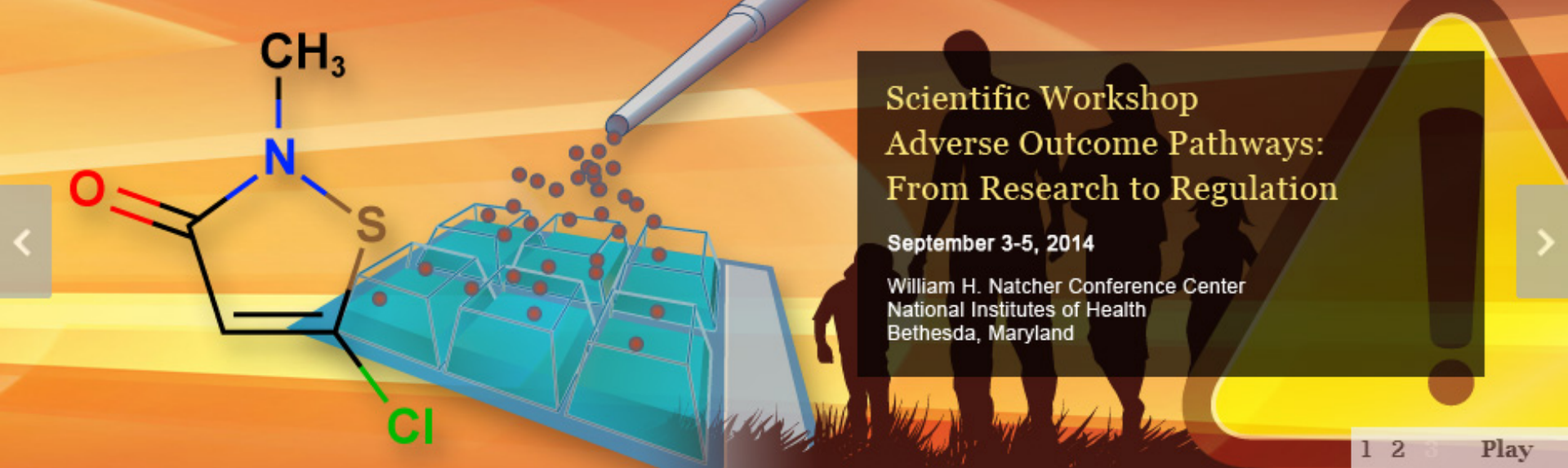
Data Quality Review

- Minimum GL-like study criteria
- Chemical/protocol/LEL information

Add to Database

- Data classified as reliable used to evaluate *in silico* and HTS results

QC: 370



Cosponsored with PCRMC, this workshop will explore how **interaction** and **collaboration** among stakeholders can be initiated and maintained so that **scientific progress** in adverse outcome pathway concepts may improve **regulatory assessment** of chemical toxicity.

Workshop Information and
Registration Page:

<http://ntp.niehs.nih.gov/go/41374>

FR Notice

- Request for available data and information on devices and/or technologies currently used for identifying potential inhalation hazards
- Information will be used to assess the state of the science and determine the technical needs for a dynamic nonanimal system to assess the potential toxicity of inhaled chemicals and nanomaterials