

US EPA ARCHIVE DOCUMENT

*Where Vision Meets Action:
Practical Application of 21st Century
Methods*

**Evolving the Endocrine Disruptor
Screening Program Case Study**

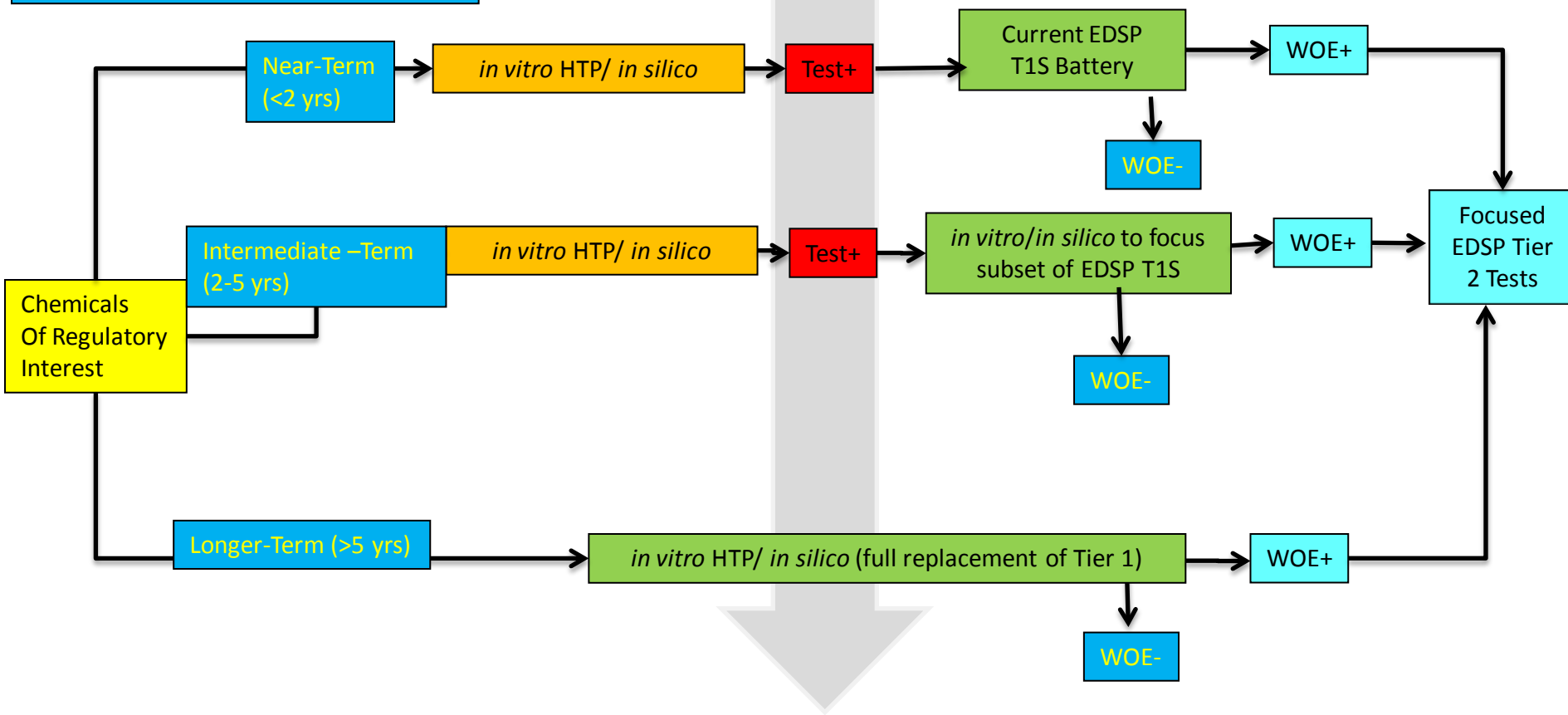
Pesticide Program Dialogue Committee
21st Century Toxicology/New Integrated Testing Strategies
Workgroup

EDSP21 Work Plan, 2011

- Evolving Incrementally while demonstrating “fit for regulatory purpose”
- Employing the Adverse Outcome Pathway as a useful scientific framework
- Maximizing use of all available data - Integrated Approaches to Testing and Assessment (IATA)
- Rigorous FIFRA Scientific Advisory Panel reviews to ensure an open and public participatory process

The universe of chemicals passes through each version of the HTP/*in silico* pipeline to evaluate chemicals in refined tests, for new pathways, to evaluate, improve, and validate methods.

EPA Research provides basis for improving the suite of assays and models to advance chemical prioritization and screening



Chemical Prioritization

Includes , registration review timeline, physico-chemical properties, exposure estimates, *in vitro* assays and computer models (QSAR, expert systems, systems biology models).

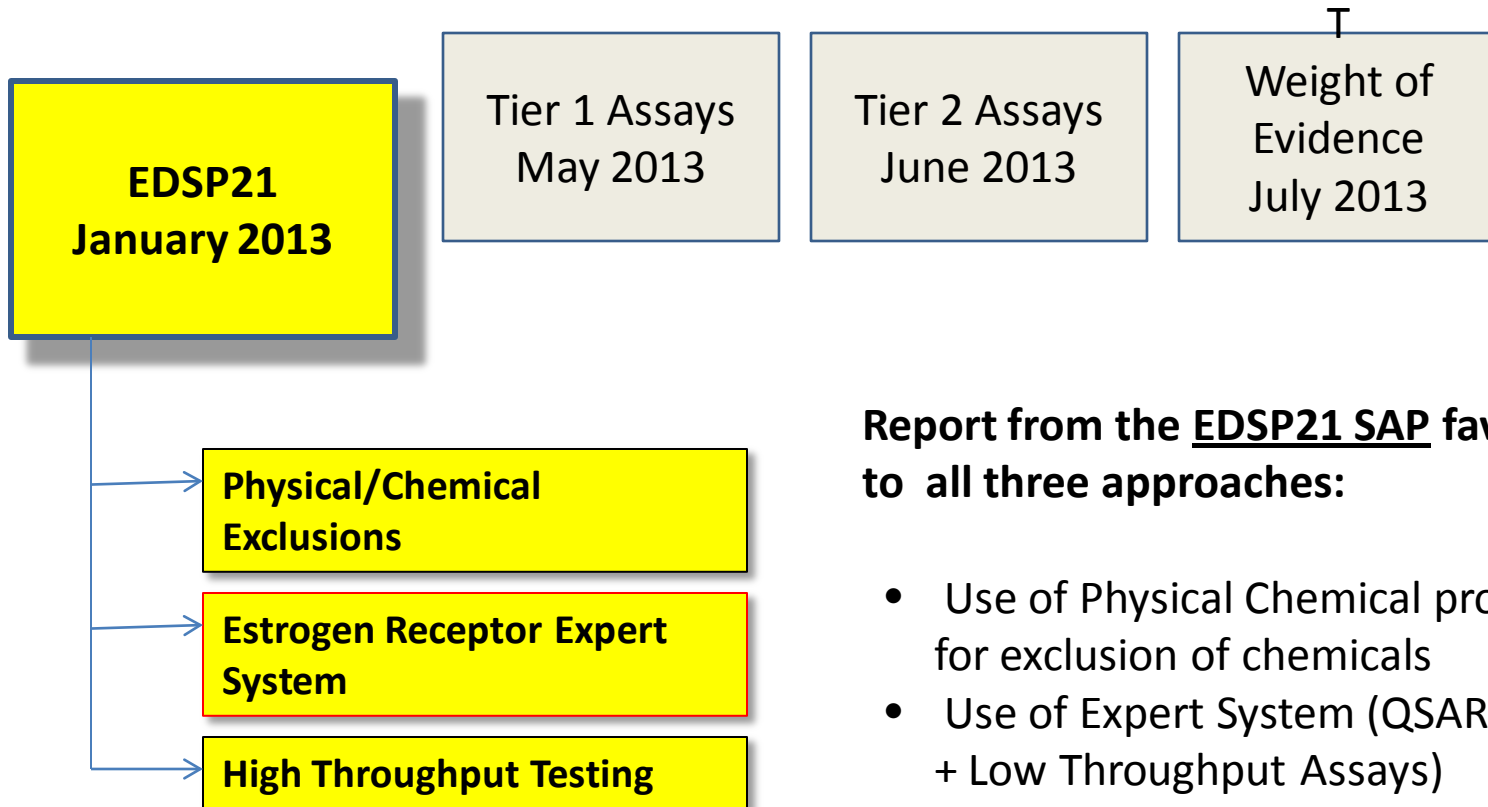
Screening Decisions

Near-Term: Incorporates HTP/*in silico* prioritization methods

Intermediate-Term: Run subset of current T1S assays indicated by HTP and *in silico* predictions

Longer-Term: Full replacement of EDSP T1S Battery

EDSP Scientific Advisory Panel Meetings 2013



Report from the EDSP21 SAP favorable to all three approaches:

- Use of Physical Chemical properties for exclusion of chemicals
- Use of Expert System (QSAR Model + Low Throughput Assays)
- Use of High Throughput ToxCast Assays

**"Prioritizing the Universe of Endocrine Disruptor Screening Program (EDSP)
Chemicals Using Computational Toxicology Tools"**

**FIFRA Scientific Advisory Panel open meeting
January 29-31, 2013**

Designated Federal Official: Dr. Sharlene Matten

FIFRA SAP Chair: Dr. Daniel Schlenk

FIFRA Advisory Panel Members:

Barry Declos

Marion Ehrich

Stephen Klaine

James McManaman

Prakesh Nagarkatti

Martha Sandy

Thomas Burris

Janice Chambers

Mark Cronin

Nancy Denslow

Miriam Jacobs

Michael Keiser

Bette Meek

Edward Perkins

Stephen Safe

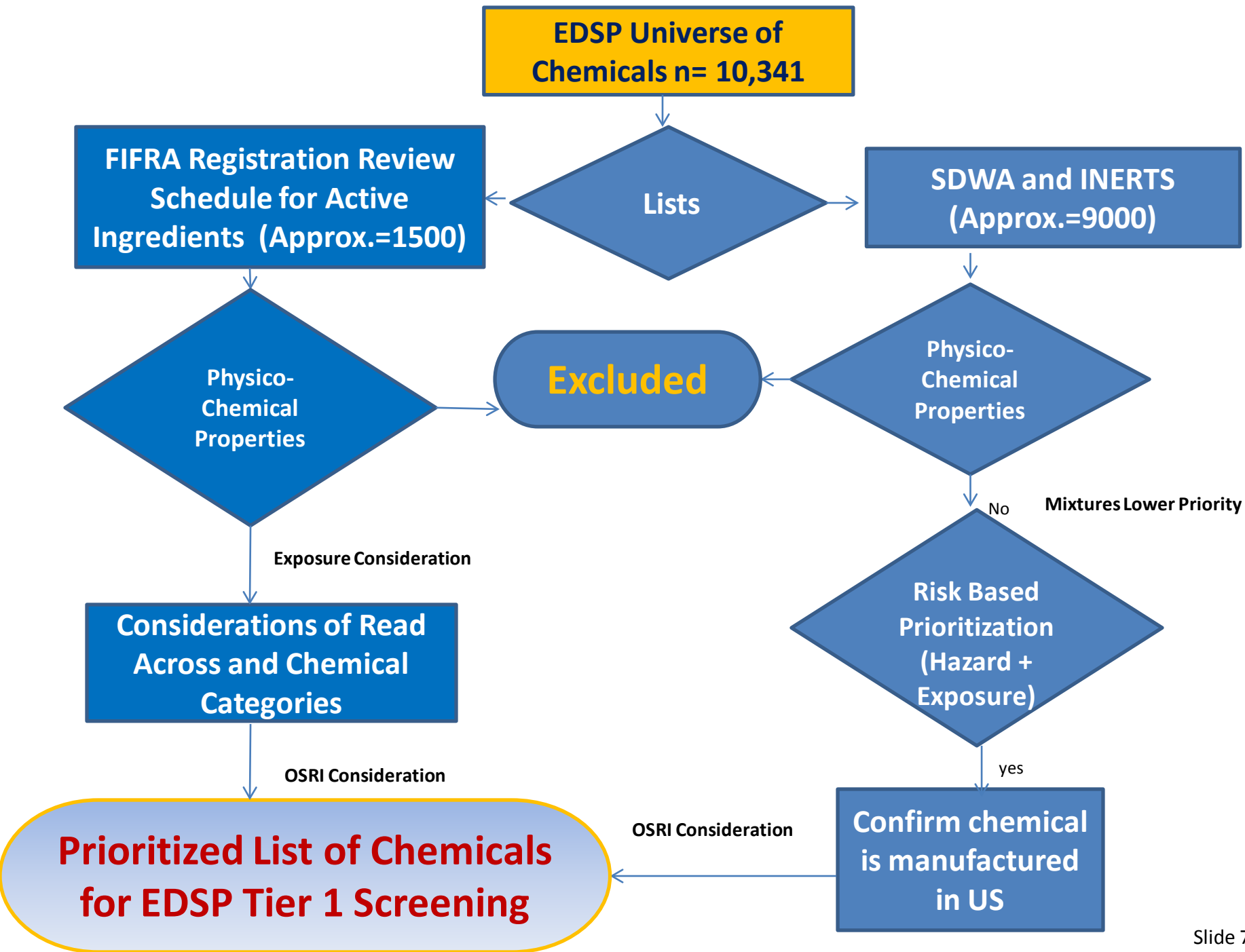
Terry Schultz

Leming Shi

Katrina Waters

SAP 2013 Key Recommendations

- Steps in the prioritization scheme were organized and clearly described, need to consider exposure earlier in the process
- Physico-chemical properties filters are founded on strong scientific principles and consistent with recommendations from 1998 EDSTAC.
- Expert System and HTP assays are potentially both useful in developing a “priority score” in combination with exposure determinations
- Other pathways: Androgen may be similar to ER pathway, but should focus on androgen antagonist. Thyroid will involve multiple modes of action that are not receptor based.



Advancing Forward

- Continue to move forward and refine approaches— Physical Chemical Properties, Expert System/High Throughput Screening based on SAP recommendations
- Update EDSP21 Workplan to reflect SAP recommendations and focus on developing a “Risk-based prioritization” approach, using both hazard and exposure data and models
- Use EDSP21 computational toxicology tools to screen chemicals across all endocrine pathways

Conceptual Framework: Strategic Testing Approach

**Risk Based Chemical
Prioritization Pre-Screen**

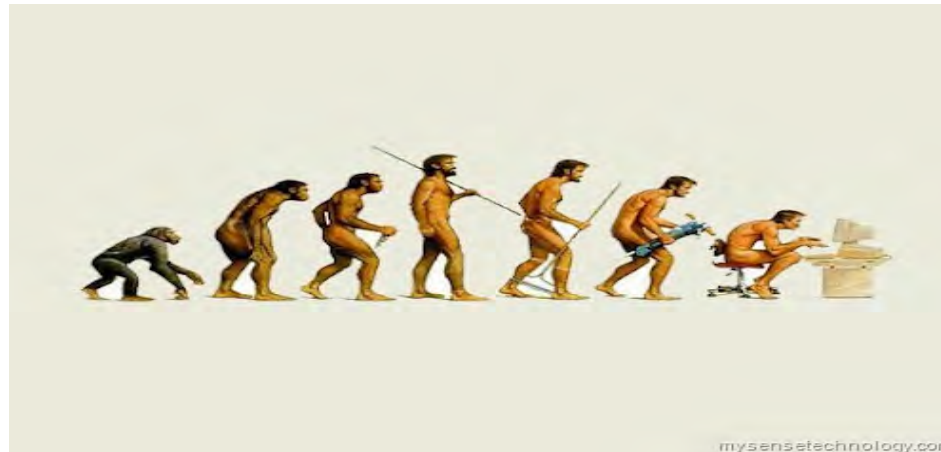
**Tier 1 Screening and
Weight of Evidence**

**Tier 2 Test
Methods**

Human Health and Ecological Impacts



Evolution of Computational Tools



“It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change.”

— [Charles Darwin](#)



Thank you!

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