

The EDMVAC Draft Work Plan

Presentation to the EDMVS,
April 26, 2005

Purpose of Today's WorkPlan

- Review the Assays
- Show progress of EDSP
- Provide the status of each assay
- Project what's next

Tier I Screening Battery

recommended for consideration by EDSTAC

- Steroidogenesis
- Pubertal - female
- Fish Screen

aka Short Term Fish Reproduction

- Amphibian Metamorphosis
- Estrogen / Androgen Receptor Binding
- Hershberger
- Uterotrophic

Alternative Assays

recommended for consideration by EDSTAC

Tier I

- Aromatase
- Pubertal male
- Adult 14 –day intact male

Tier ?

- In Utero through Lactation

Tier II Assays

recommended for consideration by EDSTAC

- Mammalian 2-generation
- Avian 2-gen. Reproduction
- Amphibian Development and Repro.
- Invertebrate (Mysid) Lifecycle
- Fish Lifecycle

Tier I Assays

Steroidogenesis

Milestone

- DRP/Protocol
 - cell based (H295R)
- Prevalidation
 - sectional testes
 - optimization
 - multichem & interlab
 - cell based (h295r)
- Validation (inter-lab)
 - Sliced testes
 - h295r

Current Status

- ✓ June 02
Dev by ORD
- ✓ June & Aug 03
Now
in lab
- to lab June 05
to lab early 06

Current Status = dates presented to EDMVS or status

Pubertals – m&f

Milestone

- DRP equivalent
- Prevalidation
 - Single Dose Study
 - Multi-chemical & multi-dose Protocols
 - Restricted Feeding Study
 - Multi-chemical & multi-dose
- Validation (inter-lab)

Current Status

- ✓ Dec 01
- ✓ Dec 01
- ✓ Dec 01
- ✓ July 02
- ✓ Dec 03
- In-life phase complete

Fish Screen

Milestones

- DRP/Protocol ✓ Mar 02
- Prevalidation
 - Fat Head Minnow protocol ✓ Mar 02
 - FHM w/multi-chemicals now
 - Comparative Study Plans: ✓ Mar 02
 - Results: Comparative Studies
Vitellogenin Methods, FHM assays ✓ Aug 03
- Validation (inter-lab)
 - Phase 1A (OECD) ✓ Aug 03
 - Phase 1B (OECD) now
 - Follow up to 1B now

Current Status

Amphibian Metamorphosis

<u>Milestone</u>	<u>Current Status</u>
■ DRP/Protocol	✓ July 02
■ Pre-validation /Validation (OECD)	
- protocol (US) demo	now
- multi-chem study	report writing
-Phase I (protocol optimization)	now
-Phase 2 Plan	now

ER Binding update

- ICCVAM - Scientific Expert Panel's May 02 retrospective validation
- EDMVS briefed by ICCVAM July 02
- ICCVAM Expert Panel Final Report Sept 02
- ICCVAM Final Report May 03
- EDSP: in lab Validation (RUC) Oct 02-June 05
- EDSP/OECD: hrER protocol optimization in lab

RUC = rat uterine cytosol

hrER = human recombinant estrogen receptor

AR Binding update

- ICCVAM Scientific Expert Panel's retrospective validation May 02
- EDMVS briefed by ICCVAM July 02
- ICCVAM Expert Panel Final Report Sept 02
- ICCVAM Final Report May 03
- EDSP: in lab prevalidation (rpc) Dec 03
- EDSP: in lab validation (rpc) in lab
- EDSP: protocol demo for rrAR future

rpc = rat prostate cytosol

rrAR = Rat recombinant androgen receptor

Aromatase

Milestones

■ DRP / Protocol

■ Prevalidation

-placental microsomal assay ✓ June 03

compare bovine, human,
porcine uterine tissue

-comparison: human placental &
recombinant, multi chem ✓ Dec 03

■ Validation (inter-lab)

Current Status

✓ Mar 02

✓ Dec 03

in lab

In Utero → Lactation

<u>Milestone</u>	<u>Current Status</u>
■ DRP -Protocol review	✓ Dec 02
■ Prevalidation -Protocol Demo -Multi-chem study	✓ Mar 02 change protocol
■ Validation (inter-lab)	TBD TBD

Tier II Assays

Mammalian 2-generation

<u>Milestone</u>	<u>Current Status</u>
■ Prevalidation	
One-gen. Ext. Protocol	✓ Dec 02
Propylthiouracil Study	✓ July 02
One-gen Ext. study	✓ June 03
■ Validation (inter-lab)	TBD

Avian 2-gen. Reproduction

Milestone

- DRP/Protocol
- Prevalidation
 - Avian Dosing Study Plan
 - Avian species Comparison
 - Avian Dose Study
 - Protocol demo
- Validation (inter-lab OECD)

Current Status

- ✓ Aug 03
- ✓ Mar 02
in draft
- Report writing
- future
- future

Amphibian Dev. & Repro.

Milestones

- DRP/Protocol
- Prevalidation
 - demonstration protocol
 - transferable protocol
 - multi-chem study
- Validation (inter-lab)

Current Status

- report in draft
- report writing
- future
- future
- future

Mysid Lifecycle

<u>Milestones</u>	<u>Current Status</u>
■ DRP/Protocol	✓ July 02
■ Prevalidation	
-draft protocol	in lab
-transferable protocol demo	in lab
-multi-chem study	future
■ Validation (inter-lab OECD)	future

Fish Lifecycle

Milestones

- DRP/Protocol ✓ Dec 02
- Prevalidation
 - protocol demo In Lab
 - multi-chem study future
- Validation (inter-lab OECD) future

Current Status

Summer 2005 (late July)

- In Utero Through Lactation simplified protocol
- General Issues, e.g. validation, chemicals, etc.

Early Fall 2005 (late Sept/early Oct)

- Avian Dosing Study
- Avian Species Comparison Study
- Adult male

Winter 2005 (end Nov/early Dec)

- Aromatase Validation
- Frog Metamorphosis multi-chem Study & Phase II
- Frog Dev / Repro Demonstration
- Pubertals
- Steroidogenesis (h295r)

EPA Docket
www.epa.gov/edocket
April 2005 OPPT-2005-0012

EDSP website
www.epa.gov/scipoly/oscpendo