

The EDMVAC Draft Work Plan

Presentation to the EDMVAC,
November 30, 2005

Purpose of Today's Work Plan

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

Tier-I Screening Battery

recommended for consideration by EDSTAC

- Steroidogenesis
- Pubertal – female rat
- 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 rat
- 15 – day adult intact male rat

Tier ?

- *In Utero* through Lactation (rat)

Tier-II Assays

recommended for consideration by EDSTAC

- Mammalian 2-generation (rat)
- 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)
 - h295r

Current Status

- ✓ June 02
- ✓ April 05
- ✓ June & Aug 03
- ✓ April 05
- Today
- Future

Current Status = dates presented to EDMVS/EDMVAC 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

Next Meeting

Fish Screen

Milestones

- DRP/Protocol
- Prevalidation /Validation (OECD)
 - Fat Head Minnow protocol
 - FHM w/multi-chemicals
 - Comparative Study Plans:
 - Results: Comparative Studies
Vitellogenin Methods, FHM assays
 - Phase 1A (OECD)
 - Phase 1B (OECD)
 - Follow up to 1B
 - Phase 2

Current Status

- ✓ Mar 02
- ✓ Mar 02
- ✓ April 05
- ✓ Mar 02
- ✓ Aug 03
- ✓ Aug 03
- ✓ April 05
- ✓ April 05
- Next Meeting

Amphibian Metamorphosis

Milestone

- DRP/Protocol
- Pre-validation /Validation (OECD)
 - protocol (US) demo
 - multi-chem study
 - Phase I (protocol optimization)
 - Phase 2 Plan
 - Phase 2 (in lab)

Current Status

- ✓ July 02
- ✓ April 05
report writing
- ✓ April 05
- ✓ April 05
on-going

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-Dec 05
- EDSP/OECD: hrER protocol optimization in lab report in 2006

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) report Jan 06
- EDSP: protocol demo for rrAR update next meeting

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

✓ June 03

✓ Dec 03

Next Meeting

15 – day adult intact male rat

- Industry lead effort with EPA support

Milestone

- Overview of Assay by Industry
- Protocol development results
(EPA sponsored 1 lab:1 chem)
& Inter-laboratory validation plan
(Industry & EPA presented
refined protocol to EDMVAC)
- Inter-laboratory validation:
EPA sponsored 3 labs: 2 chems

Current Status

- ✓ Dec 03
- ✓ Aug 05
- on-going

In Utero through Lactation

Milestone

- DRP
 - Protocol review
- Prevalidation
 - Protocol Demo with Methoxychlor
- Validation (inter-lab)

Current Status

- ✓ Dec 02
- ✓ Mar 02

Finalizing report

TBD

Tier-II Assays

Mammalian 2-generation

Milestone

- Assess added thyroid endpoints with Propylthiouracil (PTU)

Current Status

✓ July 02

- Assess abbreviated test:
 - One-gen. extension protocol
 - One-gen. extension study with vinclozolin & DBP

✓ Dec 01

✓ June 03

- Multigenerational protocol & test

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
- Today
- Today
- 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

Milestones

- DRP/Protocol
- Prevalidation
 - draft protocol
 - transferable protocol demo
 - multi-chem study
- Validation (inter-lab OECD)

Current Status

- ✓ July 02
- in lab
- in lab
- future
- future

Fish Lifecycle

Milestones

- DRP/Protocol
- Prevalidation
 - protocol demo
 - multi-chem study
- Validation (inter-lab OECD) future

Current Status

✓ Dec 02

In Lab
future

What's next

Spring 2006 (Late April / May)

- Aromatase Interlaboratory Data
- Frog Metamorphosis multi-chem Study & Phase II
- Fish Screen Phase 2 data and update
- Pubertals interlaboratory Data
- Steroidogenesis H295R next steps

Early Fall 2006

- 15-day adult intact male (by Industry)
- *In utero* through lactation
- Frog Dev / Repro Demonstration
- Mysid 2-Generation

EPA Docket
www.epa.gov/edocket
November/December 2005
EPA-HQ-OPPT-2005-0054

EPA's EDSP website
www.epa.gov/scipoly/oscpendo