US Food and Drug Administration Workshop
Reproductive and Development Toxicology Testing- From In Vivo to In Vitro

April 16, 2012
Building 31, Great Room
White Oak Campus
US Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20933

Co-Sponsored by the National Institute of Environmental Health Sciences, the Center for Alternatives to Animal Testing, Johns Hopkins University and the Middle Atlantic Reproduction and Teratology Association

Registration is free but space is limited. To register, please send your name, affiliation, and email to OCSFDAWORKSHOP@fda.hhs.gov

AGENDA

8:35 -8:45	**Welcome, and Why Are We Here?** Suzanne Fitzpatrick Office of the Commissioner
8:45-8:55	**Integration of New Drug Development Tools into the FDA Regulatory Framework** Douglas Throckmorton Center for Drug Evaluation and Research
Session I	**New In Vitro Tools for Predicting Reproductive and Developmental Toxicity- Strengths and Limitations** Chair: Abigail Jacobs Center for Drug Evaluation and Research
9:00-9:10	**Introduction to Session I: Often, the screen is plural** Chair: Abigail Jacobs Center for Drug Evaluation and Research
9:10-9:40	**Merck's battery: rat whole embryo, gene expression, and huEST lines** Diane Umbenhauer Merck

9:40 -10:05 **Zebrafish- description, applicability and limitations**
Belen Tornesi
Abbott

10:05 -10:35 **Pfizer's Battery: mEST, gene expression, Zebrafish**
Robert Chapin
Pfizer

10:35- 10:50 Break

10:50- 11:15 **How are statistical models for embryofetal development tests or batteries developed and evaluated? Why We need Rigor**
Kjell Johnson
Pfizer

11:15 –12:15 **Panel Discussion**
Moderator: Abby Jacobs
Session I Speakers plus Ed Fisher,CDER, Ben Fisher,CDRH
Jeff Bray, CDER, Deborah Hansen, NCTR

Questions to be discussed

1. How many compounds are needed to qualify any new method/battery? How many pharmacologically distinct drug classes should be represented, as well as how many drugs within a class to consider the method qualified for that class?
2. Do different differentiation pathways of stem cells need to be captured (e.g., cardiac vs neuronal vs bone?
3. What would be preferred? Human embryonic stem cell line vs mouse embryonic stem cell line vs mouse embryonic cells vs human pluripotent stem cells and why?
4. Which in vivo DART endpoints should be covered by in vitro systems? Is there a need to develop more tests for a battery?
5. What performance criteria should be used to decide if battery predicts well enough for it being acceptable to definitively test in one in vivo species?
6. What should the results of the in vitro battery be compared to?
7. Which alternative assays show the most promise? Strengths and weaknesses of those most commonly used?

12:15- 1:15 **Lunch on Your Own**

Session II	**Strategies/considerations for regulatory use** Chair: Amy Ellis Center for Drug Evaluation and Research
1:15- 1:35	**Predictivity of Current In Vivo Testing- not just a plus or minus result** Edward Fisher Center for Drug Evaluation and Research
1:35 -2:05	**It's not just black and white: in vitro, the dose still matters** George Daston Proctor and Gamble
2:05 -2:30	**Species Selection Considerations for Teratogenicity Testing: Beyond the Rat/Rabbit Default** Jeff Bray Center for Drug Evaluation and Research
2:30-2:45	**ILSI/HESI DART Project** Bruce Beyer Sanofi
2:45-3:00	**IQ consortium** Maryellen Mcnerney Bristol-Myers Squibb
3:00-3:15	**Tox 21 Update** Chris Austin NIH
3:15- 4:45	**Panel Discussion** Moderator: Amy Ellis Session II speakers plus Ed Fisher, Ben Fisher, Jeff Bray, Robert Sprando, CFSAN, Kevin Gaido, CVM

Questions to be discussed

1. What is needed to start accepting an alternative battery now in various situations? As an adjunct to in vivo? When we might only get repro/dev test results for one species, so having results from the alternative battery would add to the information we'd get for the product? To supplement one in vivo study to support phase 3 clinical trials?

2. Could there be a prescreen for applicability? What about biologics?
3. What details from the rat/rabbit EFD studies could help arrive at decisions regarding whether the alternative battery appears to be acceptable?
4. How would you resolve discordance between results in the in vitro assay and the in vivo assay?
5. What would we do if the animal embryonic cells gave us a signal and the human cells were clean?
6. How would we weigh in vitro results from cells from one animal species against results from a different animal species if they are not concordant?
7. What could be the series of steps that get us from the present to the place where an in vitro assay has replaced one species? How do we put in vitro assay results into context with in vivo exposure? (e.g., battery shows positive signal, but at relatively high concentration and systemic exposure to active ingredient in product is really low in humans)

4:45-4:50 **Closing Remarks and Next Steps**
Suzanne Fitzpatrick
Office of the Commissioner

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A Poster session will be displayed outside the conference room.

Webcasting will be available at https://collaboration.fda.gov/reprotox/

If you have never attended a Connect Pro meeting before:

Test your connection:
https://collaboration.fda.gov/common/help/en/support/meeting_test.htm

Get a quick overview: http://www.adobe.com/go/connectpro_overview

Please note- all visitors MUST park in the SE surface lot and walk or take the shuttle to Building 1. That is the only building through which they can enter. There is no "Building 31 entrance," just building 1.

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