

**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](mailto:OCSFDAWORKSHOP@fda.hhs.gov)**

**AGENDA**

- 8:35 -8:45 AM :** **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 Predicating 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- 1:00**      **Lunch on Your Own**

- Session II**                    **Strategies/considerations for regulatory use**  
Chair: Amy Ellis  
Center for Drug Evaluation and Research
- 1:00- 1:25**                    **Predictivity of Current In Vitro Testing- not just a plus or minus result**  
Edward Fisher  
Center for Drug Evaluation and Research
- 1:25 -1:55**                    **It's not just black and white: in vitro, the dose still matters**  
George Daston  
Proctor and Gamble
- 1:55 -2:25**                    **Species Selection Considerations for Teratogenicity Testing: Beyond the Rat/Rabbit Default**  
Jeff Bray  
Center for Drug Evaluation and Research
- 2:25-2:35**                    **ILSI/HESI DART Project**  
Bruce Beyer  
Sanofi
- 2:35-2:45**                    **IQ consortium**  
Maryellen Mcnerney  
Bristol-Myers Squibb
- 2:45-3:00**                    **Tox 21 Update**  
Chris Austin  
NIH
- 3:00- 4:30**                    **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)

**4:30-4:35**

**Closing Remarks and Next Steps**

Suzanne Fitzpatrick

Office of the Commissioner

**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](https://collaboration.fda.gov/common/help/en/support/meeting_test.htm)

*Get a quick overview: [http://www.adobe.com/go/connectpro\\_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.

<http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>