HESI Technical Committee

DEVELOPMENTAL AND REPRODUCTIVE TOXICOLOGY (DART)

2012-2013 Activities and Accomplishments

Committee leaders:
Dr. Wafa Harrouk
US Food and Drug Administration

Dr. Jane Stewart
AstraZeneca Pharmaceuticals

HESI manager:
Dr. Connie Chen

This scientific program is committed to:
- Providing a forum in which scientists from industry, government, and academia can exchange information;
- Initiating activities to advance science related to developmental and reproductive toxicology; and
- Developing consensus on the appropriate use of experimental toxicity data for human health risk assessment.

Areas of scientific focus:
- Developing a database of pharmaceutical developmental toxicity data from rat and rabbit species to evaluate concordance.
- Evaluating corporate policies and clinical practices for birth control methods and effectiveness in clinical trials.
- Providing a forum for alternative assay developers to assess testicular toxicity, and identifying areas of needed research and collaboration.
- Developing a list of developmental toxicants for validating alternative assays.
- Addressing the potential for female and/or conceptus exposure to drugs or biological pharmaceuticals via transfer from male sexual partners during intercourse.
- Evaluating developmental toxicity testing strategies in currently accepted animal models.

Why get involved?
- Opportunity to contribute expertise and resources to address the value of rabbit as the second test species in developmental toxicity risk assessment.
- Opportunity to develop good practice guidance on corporate policies and clinical practices for birth control.
- Opportunity to propose future developmental and reproductive toxicology (DART) workstreams that address issues of concern within your organization.

Key accomplishments:
- Testicular Toxicity. A manuscript summarizing the workshop co-sponsored by the Johns Hopkins Center for Alternatives to Animal Testing was accepted to ALTEx.
- Consensus List of Developmental Toxicants. Reached consensus on the list of compounds at the September 2012 workshop. Additional developmental toxicity and pharmacokinetic data for the compounds are currently being evaluated.
- Drugs/Biologics in Human Semen. Several experimental research projects to address data gaps and provide supporting evidence for modeling exposure scenarios are nearing completion.
• Second Species. Issued a call-for-data; the data are being anonymized and collected into a database for further evaluation.
• Birth Control in Clinical Studies. A survey to collect information on contraception use during clinical trials has been developed and distributed.

The Committee's focus for May 2013 - May 2014:
• Complete the Drugs/Biologics in Human Semen laboratory research projects and publish the manuscript.
• Complete the second-species developmental toxicology database.
• Complete data collection and analysis for the survey on contraception requirements during clinical trials.
• Publish manuscripts for the Consensus List of Developmental Toxicants project.

Recent publications:
• Chapin RE, Kim JH. Introduction to the HESI-sponsored inhibin consortium. pp 1–3.
• Moffit JS, et al. Assesment of inhibin B as a biomarker of testicular injury following administration of carbendazim, cetrotrelax, or 1,2-dibromo-3-chloropropane in Wistar Han rats. pp 17–28.
• Breslin WJ, et al. The inhibin B (InhB) response to the testicular toxicants mono-2-ethylhexyl phthalate (MEHP), 1,3 dinitrobenzene (DNB), or carbendazim (CBZ) following short-term repeat dosing in the male rat. pp 72–81.
• Chapin R, et al. Summary of the HESI consortium studies exploring circulating inhibin B as a potential biomarker of testis damage in the rat. pp 110–118.

2012 - 2013 Participating organizations:
Abbott Laboratories
AbbVie, Inc.
Alkermes Inc.
Altimira LLC
Amgen Inc.
AstraZeneca Pharmaceuticals
Battelle Memorial Institute
Bayer HealthCare Pharmaceuticals
Beckman Coulter
Belgian Federal Agency for Medicines and Health Products
Boehringer Ingelheim Pharmaceuticals Inc.
Bristol-Myers Squibb Company
Celgene Corporation
Charles River Laboratories
Covance Inc.
Creighton University School of Medicine
DuPont
Eli Lilly and Company
E'ponent
ExxonMobil Biomedical Sciences, Inc.
F. Hoffman-La Roche Ltd.
GlaxoSmithKline
Janssen Pharmaceuticals
McMaster University
Medical Products Agency (Sweden)
Medicines and Healthcare Products Regulatory Agency (UK)
Merck & Co. Inc.
National Institute for Public Health and the Environment (RIVM, The Netherlands)
Novartis Pharmaceuticals Corporation
Pfizer Inc.
RTI International
Sanofi
Takeda Pharmaceutical Company Limited
Tetra Tech Sciences
The Dow Chemical Company
The Procter & Gamble Company
University of British Columbia
University of Washington
US Environmental Protection Agency
US Food and Drug Administration

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