RISK ASSESSMENT FOR SENSITIVE POPULATIONS SUBCOMMITTEE

Mission

The mission of the HESI Subcommittee on Risk Assessment for Sensitive Populations is to broaden and increase knowledge about the characterization of sensitive populations, understand efforts to apply current and proposed methods for assessing risks to sensitive populations, and integrate results from applications and lessons learned to improve risk assessment for diverse sensitive populations in the future.

2008 Participants

Alfred I. duPont Hospital for Children
Bayer CropScience
Dow AgroSciences
European Food Safety Authority (EFSA)
Federal Institute for Drugs and Medical Devices – BfArM
Medical College of Wisconsin
Monsanto Company
National Cancer Institute
National Institute of Environmental Health Sciences
University of Aarhus (Denmark)
US Environmental Protection Agency
- National Center for Computational Toxicology
- National Health and Environmental Effects Research Laboratory

US Food and Drug Administration
- Center for Drug Evaluation and Research
- National Center for Toxicological Research

Subcommittee Publication

Hines, RN, Sargent, D, Birnbaum, LS, Brent, RL, Doerrer, NG, Cohen Hubal, E, Juberg, DR, Laurent, C, Luebke, R, Olejniczak, K, Portier, C, Slikker, W. 2010. Approaches for assessing risks to sensitive populations: lessons learned from evaluating risks in the pediatric population. Toxicol Sci. 113, 4-26.

Fact Sheet

ILSI Health and Environmental Sciences Institute

EMERGING ISSUES SUBCOMMITTEE ON RISK ASSESSMENT FOR SENSITIVE POPULATIONS

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BACKGROUND

Sensitive populations result from age, medical conditions, genetics, and socioeconomic status. Because current risk assessments are based largely on exposures in young, healthy adults, they may fail to provide adequate evaluation of health risks for sensitive populations. In recognition of these concerns, the HESI Scientific Map identifies issues relating to assessment of sensitive populations as important areas for HESI focus in the future.

From a regulatory risk assessment perspective, sensitive populations are the focus of increased attention to mode-of-action research, pharmacokinetics investigations, age-specific issues, and genetic susceptibility assessment among other areas.

OBJECTIVES

The Subcommittee will consider the following questions:

- What scientific considerations should be included in defining or characterizing a sensitive population (e.g., exposure, physiologically-based pharmacokinetics, etc.)?
- What is the adequacy of and/or gaps in current and proposed procedures and approaches to assess risk in sensitive populations (using children as an initial example of a sensitive population)?
- Can existing procedures and approaches to assessing risk in sensitive populations be extrapolated across different population types? If not, where are there needs for modification of these approaches?

The results of the analysis of these questions will result in white papers, peer-reviewed publications, and/or workshops.

ACCOMPLISHMENTS

- The Subcommittee was initiated in the summer of 2006 as part of HESI's Emerging Issues process. The Subcommittee convened for the first time in October 2006 in Washington, DC. The meeting resulted in a defined mission and proposed work plan for the Subcommittee.
- The Subcommittee organized a scientific session on sensitive populations as part of the January 2007 HESI Annual Meeting.
- During 2007, the Subcommittee set and achieved the following goals: 1) identified and gained familiarity with current published scientific literature (and published regulatory documents) that relate to the evaluation of risk to children as an example of a well studied

subpopulation, and b) used the information from this review to begin identifying methodological approaches for assessing risk to children and determining how/if these approaches might be relevant to other types of subpopulations.

- In 2008, a manuscript was developed to guide discussion within the scientific and regulatory communities on three fundamental questions: (1) What scientific issues need to be considered in defining and characterizing a sensitive subpopulation? (2) What scientific data gaps exist in the procedures and approaches for assessing risk in sensitive populations? and (3) Can existing procedures and approaches for assessing risk in children as a sensitive subpopulation be extrapolated to other populations? In the manuscript, four major scientific factors relating to childhood susceptibility are discussed: pharmacokinetics, pharmacodynamics, genetics, and exposure. In each of these areas, lessons learned from methods used to assess children's risks translate to approaches that could be used to identify and characterize other sensitive populations.

FUTURE ACTIVITIES

The Subcommittee's manuscript on "Approaches for Assessing Risks to Sensitive Populations: Lessons Learned from Evaluating Risks to Children" will be submitted for publication in early 2009 in a scientific, peer-reviewed journal.

The Subcommittee will officially "sunset" after publication of the manuscript in the open literature.

ANTICIPATED IMPACT

This multi-sector activity is well timed to provide input into evolving approaches for the risk assessment of sensitive populations.

LEADERSHIP AND INFORMATION

Chair .....Dr. Ronald Hines
(Medical College of Wisconsin)
Vice Chair..... Dana Sargent, MS
(Bayer CropScience)
HESI Staff ..... Nancy G. Doerrer, MS
Ms. Regina Graham

For more information, contact:
Nancy G. Doerrer, MS
at 202-659-3306 or ndoerrer@hesiglobal.org.

SUBCOMMITTEE MEMBERSHIP

3M Pharmaceuticals
Bayer CropScience
Dow AgroSciences
Monsanto Company

PUBLIC PARTICIPATION

Alfred I. duPont Hospital for Children
European Food Safety Authority
Medical College of Wisconsin
Federal Institute for Drugs and Medical Devices (BfArM)
National Institutes of Health
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University of Aarhus, Denmark
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US Food and Drug Administration
- Center for Drug Evaluation and Research
- National Center for Toxicological Research

01/09

January 19, 2009: Risk Assessment for Sensitive Populations Subcommittee Presentation.
"Risk Assessment for Sensitive Populations." Presented at the 2009 HESI Annual Meeting. Tucson, Arizona. Presentation by Dr. Ronald Hines, Medical College of Wisconsin.

HESI Subcommittee on Risk Assessment for Sensitive Populations

Co-Chairs:

Ronald Hines, PhD

(Medical College of Wisconsin)

Dana Sargent, MS

(Bayer CropScience)

January 20, 2009, Emerging Issues Meeting

HESI Annual Meeting

Tucson, AZ

HESI Subcommittee on Risk Assessment for Sensitive Populations

- **Spring 2006**: Topic selected by HESI Emerging Issues Steering Committee
- **Fall 2006**: Subcommittee kick-off meeting
- **Work product**: Manuscript to be submitted for publication in peer-reviewed journal

Mission

- Broaden and increase knowledge about the characterization of sensitive populations.
- Understand efforts to apply current and proposed methods for assessing risks to sensitive populations.
- Integrate results from applications and lessons learned to improve risk assessment for diverse sensitive populations in the future.

2008 Subcommittee Participation

INDUSTRY

3M Pharmaceuticals
Bayer CropScience
Dow AgroSciences
Monsanto Company

PUBLIC

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Federal Institute for Drugs and Medical Devices (BfArM)
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- National Center for Toxicological Research

Manuscript

APPROACHES FOR ASSESSING RISKS TO SENSITIVE POPULATIONS: LESSONS LEARNED FROM EVALUATING RISKS IN THE PEDIATRIC POPULATION

Ronald N. Hines[1], Dana Sargent[2], Herman Autrup[3], Linda S. Birnbaum[4], Robert L. Brent[5], Nancy G. Doerrer[6*], Elaine Cohen Hubal[4], Daland R. Juberg[7], Christian Laurent[8], Robert Luebke[4], Klaus Olejniczak[9], Christopher J. Portier[10], William Slikker[11]

(targeted journal: *Environmental Health Perspectives*)

Scientific Manuscript: Four Fundamental Issues

1. Identification of critical biological, toxicological, and exposure-related factors that should be examined when evaluating vulnerability (in this case, in the pediatric population).

2. Identification of methods, models, and experimental designs for evaluating pediatric populations which may be useful in evaluating other populations.

3. Identification of parameters unique to the pediatric population and that are not useful for extrapolating to other groups.

4. Identification of key gaps in the pediatric/vulnerability literature that should be addressed for pediatric and other potentially vulnerable groups.

Major Topics in Manuscript

- Consideration of pediatric subjects as a sensitive population model when evaluating other potentially vulnerable groups
- Defining a sensitive population
- Relevant factors in the identification and assessment of sensitive populations (e.g., pharmacokinetics, pharmacodynamics, genetics, environmental exposure)
- Biomarkers of susceptibility
- Implementation of population-specific factors in risk assessment / modeling
- Discussion

Approach and Timeline

- **July 2007 - Subcommittee selected published literature for review.**
- **September 2007- Subcontractor was retained to review literature and produce summaries and commentaries regarding utility.**
- **December 2007 - Subcommittee developed a manuscript outline.**
- **January 2009 - Manuscript completed and submitted for HESI peer review.**
- **February 2009 - Manuscript submitted for publication in a scientific peer-reviewed journal (*EHP*).**

Next Steps

- Sunset the Subcommittee after submission of manuscript to peer-reviewed journal (early 2009).

- The HESI Emerging Issues Steering Committee (EISC) could consider convening a more focused group on this topic when and if a proposal is submitted in future years through the annual emerging issues survey.