HESI

Emerging Issues Subcommittee

Methodology for Intermittent and Short-Term Exposure to Carcinogens (MISTEC)

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Tucson, Arizona

Mission Statement

Develop methodology for establishing appropriate dose metrics to assess the potential carcinogenic risk to humans following short-term or intermittent exposures to chemicals based on current understanding of the carcinogenic process, and using data from experimental studies in animals, observational studies in humans, *in silico* data and mechanistic studies. Data gaps will be identified and relevant research proposed.

History

- Topic selected by EISC in January 2008
- Subcommittee kick-off meeting October 2008

2008 SUBCOMMITTEE PARTICIPATION

LEADERSHIP

Susan P. Felter, PhD
(Procter & Gamble Company)

Gary M. Williams, MD, DABT
(New York Medical College)

INDUSTRY

Dow Chemical Company
Johnson & Johnson Pharmaceuticals

PUBLIC

Imperial College London
Michigan State University
National Institute for Public Health and the Environment (RIVM)
University of Arizona
US Environmental Protection Agency
    National Center for Computational Toxicology
    Office of Water
US Food and Drug Administration
    Center for Drug Evaluation and Research

Objectives

- Obtain and critically evaluate available literature on the topic of assessing risk from short-term and/or intermittent exposure to carcinogens.

- Define the scope of this project in terms of known modes of action for carcinogens (particularly for those MOAs associated with a threshold versus those that are not).

Objectives (cont'd)

- Define "short-term" and "intermittent" exposure, particularly as distinguished from "chronic, lifetime" exposure for the purposes of quantitative cancer risk assessment. Determine whether various exposure durations can be represented by "tiers."
  - Determine if these definitions should be modified based on type of chemical (e.g., long half-life vs. short half-life), life stage at time of exposure, or other criteria.

Objectives (cont'd)

- Based on the scope of the project, develop recommendations for a quantitative approach (including the most appropriate dose-metric) to assessing risk. Principles of this approach include:
  - Transparency, consistency, pragmatism and health-protection.
  - Consider all possible approaches (e.g., linear low-dose extrapolation, margin-of-exposure approach, potency considerations, etc).

Objectives (cont'd)

- Identify research that can be conducted using existing/emerging technologies that might help fill data gaps associated with or improve our understanding of questions of exposure duration (i.e., modeling approaches, dose-surrogates, and biomarkers).

Approach and Timeline

- Following a teleconference, the Steering Team held its first meeting on October 10, 2008.
- The draft mission statement and subcommittee objectives were developed and are under review.
- Additional subcommittee participants will be invited on an as-needed basis.
- All interested parties will be invited to attend a formal workshop in June 2009 (tentative).

Next Steps

- Finalize the mission statement and objectives via email and conference calls by February 2009.
- Begin to draft methodology for workshop.
- Next face-to-face meeting will be held March 5-6, 2009 in Washington, D.C.

MISTEC Timeline

TIMELINE	
January 2008	January 2008 HESI Annual Meeting Presentation
Summer 2008	Build Steering Team
September 10, 2008	Hold introductory Steering Team conference call
October 2008	Steering Team meeting at HESI offices
November 2008 – February 2009	Follow-up conference calls to prepare for full Subcommittee meeting
March 5-6, 2009	Subcommittee meeting at HESI offices
March – May 2009	Prepare for 1st workshop
June 2009	Hold 1st workshop to review the 'state of the science'
July 2009	Review and discuss workshop outcome and results
August 2009	Begin drafting white paper scope and outline
August – September 2009	Draft 1st drafts of white paper sections
October – November 2009	Prepare white paper for HESI peer review
December 2009 – January 2010	White paper HESI peer review
February – April 2010	White paper publication