Introduction

Welcome to the EPA Human Studies Review Board (HSRB)!

This presentation is designed to provide new members with comprehensive information about the HSRB. It is also meant to serve as an ongoing resource for all HSRB members.

- New members are encouraged to review all components of this orientation.
- Existing members are encouraged to refer to this package for answers to questions concerning HSRB operations.
- Much of the information contained in this orientation package, as well as additional documents and information, are available at the HSRB web site.

Click here for the link to the Human Studies Review Board

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About the HSRB

- On February 6, 2006 the Agency published a final rule for protections of subjects in human research that called for creating a new, independent human studies review board and described its responsibilities in the following language:
- "The Human Studies Review Board shall comment on the scientific and ethical aspects of research proposals and reports of completed research with human subjects submitted by EPA for its review and on request, advise EPA on ways to strengthen its programs for protection of human subjects of research."
- EPA's Human Studies Review Board (HSRB) was chartered by Congress on February 21, 2006 (and subsequently rechartered effective March 4, 2008) to provide advice, information, and recommendations on issues related to scientific and ethical aspects of human subjects research. The HSRB operates in accordance with the provisions of the Federal Advisory Committee Act (FACA), 5 U.S.C. App.2 §.
- HSRB's major objectives are to provide advice and recommendations on:
  - Research proposals and protocols
  - Reports of completed research with human subjects
  - How to strengthen EPA's programs for protection of human subjects of research

Click here for the link to the Human Studies Review Board Charter

Click here for the link to the Protections for Subjects in Human Research: Final Rule

HSRB Organization

The HSRB is housed within The Program in Human Research Ethics (PHRE) which is located under EPA's Office of the Science Advisor.

Director, PHRE

- Warren Lux serves as the Director of the PHRE.
- He can be reached at (202) 564-3746 or by email at lux.warren@epa.gov.

Executive Director, HSRB

- Jim Downing serves as Executive Director of the HSRB, responsible for overall management of the HSRB, and is also the Designated Federal Official (DFO) to the Board.
- He may be reached at (202) 564-2468 or by email at downing.jim@epa.gov.

Program Analyst, PHRE

- Lu-Ann Kleibacker serves as a Program Analyst.
- Lu-Ann is responsible for providing programmatic support to PHRE and the HSRB, including assisting HSRB members with their travel and logistics.
- She may be reached at (202) 564-7189 or by email at Kleibacker.lu-ann@epa.gov.

History Leading to HSRB Establishment

1996: Food Quality Protection Act (FQPA)

- Passage of FQPA raised concerns about possible increase in submission of research with human subjects involving intentional dosing with a pesticide to identify or measure a toxic effect.

1998: EPA Statement on Pesticide Human Studies

- "No human test data has been used by EPA for any final decisions about acceptable levels of pesticide under the new food safety law [FQPA]."

Click here for the link to EPA's statement

1998: Data from Testing of Human Subjects Subcommittee

- EPA convened a joint advisory committee meeting of EPA's Science Advisory Board and Scientific Advisory Panel to address issues on the scientific and ethical acceptability of research with human subjects involving intentional dosing with a pesticide to identify or measure a toxic effect.

- While the committee agreed unanimously on several broad principles, no clear consensus emerged on many other points, including both the scientific merit and ethical acceptability of studies to identify or measure toxic effects of pesticides in human subjects.

The report of Data from Testing of Human Subjects Subcommittee

History Leading to HSRB Establishment (continued)

2001:

- EPA asks the National Academy of Sciences (NAS) to provide advice on scientific and ethical issues of intentional human dosing studies for regulatory purposes. EPA asked NAS whether and under what circumstances EPA should accept and consider intentional human dosing studies conducted by companies or other sources outside the Agency (i.e. third-party research).
- As part of the process, EPA issued a press release stating, "during the Academy's consideration of the issues and until a policy is in place, the Agency will not consider or rely on any such human studies [third-party studies which intentionally dose human subjects with toxicants to identify or quantify their effects] in its regulatory decision making, whether previously or newly submitted."

EPA Press Release

2002-2003: Lawsuit Against EPA Press Release

- Various parties from the pesticide industry filed suit regarding EPA's press release, arguing it constituted a "rule" promulgated in violation of the Administrative Procedures Act and the Federal Food, Drug and Cosmetic Act.
- The U.S. Court of Appeals for the D.C. Circuit agreed with the plantiffs, vacating the Agency's directive and reinstating that EPA's previous practice of considering third-party human studies on a case-by-case basis. The court ordered the practice to remain reinstated and remains in effect unless and until it is replaced by a lawfully promulgated regulation.

Full Text of the Court's Decision (PDF) (7pp, 158K, About PDF)

2003: EPA issued an Advance Notice of Proposed Rulemaking on Human Testing

- EPA issued an advance notice of proposed rulemaking on human testing, announcing its intention to undertake notice-and-comment rulemaking on the subject.

Advanced Notice of Proposed Rulemaking

History Leading to HSRB Establishment (continued)

2004: NAS releases report.

- The NAS recommended that intentional human dosing studies be conducted and used for regulatory purposes only if all of several strict conditions were met, including the following:
  - The study is necessary and scientifically valid, meaning that it addresses an important regulatory question that can't be answered with animal studies or non-dosing human studies.
  - The societal benefits of the study outweigh any anticipated risks to participants.
  - All recognized ethical standards and procedures for protecting the interests of study participants are observed.
- In addition, the NAS suggested that EPA establish a human studies review board to evaluate all human dosing studies – both at the beginning and upon completion of the experiments – if they are carried out with the intent of affecting the Agency's policy-making.

National Academies of Science Report EXIT Disclaimer

2005: EPA announces plan to establish a comprehensive framework for deciding whether to consider or rely on certain types of research with human subjects

Federal Register notice announcing the plan

History Leading to HSRB Establishment (continued)

2005: 2006 Appropriations Act

- On August 2, 2005, President Bush signed into law the Department of Interior, Environment, and Related Agencies Appropriations Act (the Act).
- The Act appropriated funds for the EPA and certain other Federal departments and agencies.
- Section 201 of the Act included the following provision:

  "None of the funds made available by this Act may be used by the Administrator of the Environmental Protection Agency to accept, consider or rely on third-party intentional dosing human toxicity studies for pesticides, or to conduct intentional dosing human toxicity studies for pesticides until the Administrator issues a final rulemaking on this subject. The Administrator shall allow for a period of not less than 90 days for public comment on the Agency's proposed rule before issuing a final rule. Such rule shall not permit the use of pregnant women, infants or children as subjects; shall be consistent with the principles proposed in the 2004 report of the National Academy of Sciences on intentional human dosing and the principles of the Nuremberg Code with respect to human experimentation; and shall establish an independent Human Subjects Review Board. The final rule shall be issued no later than 180 days after enactment of this Act."

Department of Interior, Environment, and Related Agencies Appropriations Act, 2006 (PDF) (66 pp, 395K, About PDF) EXIT Disclaimer

History Leading to HSRB Establishment (continued)

2005: EPA published Protections for Subjects in Human Research – Proposed Rule

- EPA's proposal included:
  - Prohibiting intentional exposure research on pregnant women or children intended for submission to EPA under the pesticide laws.
  - Extending new protections to adult subjects in intentional dosing human studies for pesticides conducted by others who intend to submit the research to EPA.
  - Formalizing and further strengthening existing protections for subjects in human research conducted or supported by EPA.
  - Creating a new, independent Human Studies Review Board to advise the Agency on the ethical and scientific issues arising in such research.

Proposed rule (PDF) (30 pp, 538K, About PDF)

History leading to HSRB establishment (continued)

2006: EPA published Protections for Subjects in Human Research – Final Rule

Overview of Final Rule

- Prohibits research involving intentional exposure of pregnant or nursing women or children, intended for submission to EPA under the pesticide laws.
- Extends provisions of the Federal Policy for the Protection of Human Subjects of Research to other human research involving intentional exposure of non-pregnant adults intended for submission to EPA under the pesticide laws.
- Provides additional protections for subjects in research conducted or supported by EPA.
- Creates a new, independent Human Studies Review Board to advise the Agency on the ethical and scientific issues arising in such research.

History leading to HSRB establishment (continued)

2006: EPA publishes Protections for Subjects in Human Research – Final Rule (continued)

Specifics of Final Rule

Definitions

- **Intentional exposure**
  – exposure a human subject would not have experienced had they not participated in the research.
- **Third-party research**
  – research not conducted or supported by EPA.
- **Post-rule**
  – after the date that the rule was finalized (i.e., after April 7, 2006).

EPA Conducted or Supported Research

- Prohibition of EPA research involving intentional exposure of pregnant or nursing women or children under 18.
- Additional protections for pregnant or nursing women or children under 18 even if not involved in intentional exposure research.

Third-Party Human Research for Pesticides Involving Intentional Exposure

- Established basic ethical requirements for new third-party research for pesticides involving intentional exposure.
- Prohibits new research involving intentional exposure of pregnant or nursing women or children, intended for submission to EPA under the pesticide laws.
- Review of proposed and completed human research submitted to EPA under the pesticide laws.
  - Proposed Research
    - EPA shall review all protocols.
    - Following initial EPA evaluation of the protocol, EPA submits protocol, EPA evaluation and supporting materials to HSRB for review.
  - Completed Research

History leading to HSRB establishment (continued)

- EPA shall submit its review to the HSRB if it decides to rely on the data under the pesticide laws and
  - Data are derived after April 7, 2006 or
  - Data are derived before April 7, 2006 and the research was conducted for the purpose of identifying or measuring a toxic effect.

- Ethical Standards for the Use of Any Human Data in Actions Taken by EPA under the Pesticide Laws.
  - Absolute prohibition of reliance on data from human research involving children and pregnant and nursing women.
  - Prohibition of reliance on data from human research with non-pregnant adults conducted before April 7, 2006 *if* there is clear and convincing evidence that the conduct of the research
    - was fundamentally unethical or
    - was significantly deficient relative to the ethical standards prevailing at the time the research was conducted.
  - Prohibition of reliance on data from human research with non-pregnant adults conducted after April 7, 2006 *unless*
    - EPA has adequate information to determine that the research was conducted in substantial compliance with the Final Human Studies Rule, or
    - for research conducted in a foreign country, the research was subject to procedures at least as protective as those in the Final Human Studies Rule.

- Criteria and Procedures for Decisions to Protect Public Health by Relying on Otherwise Unacceptable Research
  - EPA may rely on such research if all of the following conditions are met
    - EPA has obtained the views of the HSRB concerning the proposal to rely on otherwise unacceptable data.
    - EPA has provided an opportunity for public comment.
    - EPA has determined that relying on the data is crucial to a decision that would impose a more stringent regulatory restriction that would improve protection of public health.
    - EPA publishes a full explanation of its decision, including a thorough discussion of the ethical deficiencies of the underlying research and the full rationale for finding that the standard above was met.

Human Studies Review Board

- Establishment and operation of the HSRB in terms of membership and responsibilities.

Final Rule

2006: First meeting of Human Studies Review Board

The first HSRB meeting (DOC) (4 pp, 47K)

Important Milestones in the Development of Codes of Research Ethics

Nuremberg Code

- First set of principles outlining professional ethics for medical researchers that must be observed in order to satisfy moral, ethical, and legal concepts in the conduct of human participant research.
    1. The voluntary consent of the human subject is absolutely essential.
    2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
    3. The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
    4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
    5. No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
    6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
    7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
    8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
    9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
    10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Nuremberg Code

Important Milestones in the Development of Codes of Research Ethics

Declaration of Helsinki

- First significant effort of the medical community (World Medical Association) to regulate itself.
- Has been revised 5 times since its inception in 1964.
- Highlights
  - Respect for the individual.
  - The right of the individual to make informed decisions a central requirement.
  - Investigator's duty is solely to the patient.
  - Subject's welfare must always take precedence over the interests of science and society.
  - Ethical considerations must always take precedence over laws and regulations.
  - Surrogate consent is permitted when the research participant is incompetent, physically or mentally incapable of giving consent, or a minor.

Declaration of Helsinki EXIT Disclaimer

Belmont Report

- Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to identify ethical principles for all Federally funded research involving human subjects.
- Commission established due to increased public concern about research abuses of Federally funded biomedical research.
- In 1979 the Commission issued its report, *Ethical Principles and Guidelines for the Protection of Human Subjects* ("The Belmont Report").
- Conclusions
  - Basic Ethical Principles
    - Respect for persons
      - Individuals treated as autonomous agents.
      - Persons with diminished capacity may need additional protections.

Important Milestones in the Development of Codes of Research Ethics

- Beneficence
  - Do no harm.
  - Maximize benefits and minimize possible harm.
- Justice
  - Participants treated fairly.
  - Raises question of "Who ought to receive the benefit of the research and bear the burdens?"

- Application of general principles to research
  - Informed consent.
  - Assessment of risks and benefits.
  - Subject selection.

Belmont Report EXIT Disclaimer

Important Milestones in the Development of Codes of Research Ethics

Federal Policy for the Protection of Human Subjects (the "Common Rule")

Overview of Common Rule

- Based on principles from the Belmont Report establishing rules for research involving human subjects.
- Governs research with human subjects conducted or supported by 17 federal departments and agencies, including EPA.
- Is codified at Subpart A of DHHS Regulation 45 CFR 46 and is found at Subpart A of EPA Regulation 40 CFR 26.
- Established a comprehensive framework for the review and conduct of proposed human research to ensure that it will be performed ethically.
- The central requirements of the Common Rule are:
    - That people who participate as subjects in covered research are selected equitably and give their fully informed, fully voluntary written consent.
    - That proposed research be reviewed by an independent oversight group referred to as an Institutional Review Board (IRB), and approved only if risks to subjects have been minimized and are reasonable in relation to anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result.

Important Milestones in the Development of Codes of Research Ethics

Federal Policy for the Protection of Human Subjects (the "Common Rule")

Specifics of Common Rule

Definitions

- **Research**
  "...systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge"
- **Human subject**
  "...a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information"
- **Minimal risk**
  "...the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance or routine physical or psychological examinations or tests"

Exempted Research

- Some research is exempt from Federal regulations including:
  - Normal educational practices.
  - Educational tests, surveys, interviews, or observation of public behavior unless identified and sensitive.
  - Research using existing data, documents, records, pathological specimens, or diagnostic specimens, if publicly available or if de-identified.
  - Taste and food quality evaluation and consumer acceptance studies.

Assuring Compliance

- Documentation of institutional commitment to comply with the Common Rule is known as an assurance and is required from each institution engaged in human subjects research funded by a Federal Common Rule agency.
- A Federalwide Assurance submitted and approved by the DHHS Office of Human Research Protections may be accepted

by any Common Rule agency and is the standard assurance used by EPA.

EPA's FWA EXIT Disclaimer

Institutional Review Boards

- Review and approve, require modifications, or disapprove all covered research.
- Require that informed consent is in accordance with regulations.
- Require documentation of informed consent or may waive documentation in accordance with regulations.
- Notify investigators in writing of decisions.
- Conduct continuing review of research no less than once per year.
- Provide expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

Criteria for IRB Approval of Research

- Risks to subjects are minimized.
- Risks to subjects are reasonable in relation to anticipated benefits.
- Selection of subjects is equitable.
- Informed consent is sought from each prospective subject or subject's legally authorized representative.
- Informed consent is appropriately documented.
- When appropriate:
    - Data collection is monitored to ensure subject safety.
    - Additional safeguards are included for vulnerable populations.

Informed Consent

General Requirements

- Subject has the legal and mental capacity to give consent, or through legally authorized representative.
- Sufficient opportunity is provided to consider participation.
- The possibility of coercion or undue influence is minimized.
- Language is understandable to the subject.
- No exculpatory language.

Basic Elements

- Study involves research
  - A. Purpose.
  - B. Duration of subject's participation.
  - C. Procedures.
  - D. Identification of those procedures that are experimental.
- Description of
  - A. Foreseeable risks or discomforts.
  - B. Benefits to the subject or others which may reasonably be expected.
  - C. Confidentiality of records.
  - D. Appropriate alternative procedures.
  - E. Whom to contact about the research.
  - F. Right to refuse or withdraw from the research.
- Research involving more than minimal risk, must include an explanation of
  - A. Whether there will be any compensation.
  - B. Medical treatment available if injury occurs.

Additional Elements

- Treatment may involve unforeseeable risks.
- Termination of subject's participation without regard to subject's consent.

- Additional costs to the subject.
- Consequence of withdrawal.
- Informing subject of new findings.
- Number of subjects.

Waiver of Consent

An IRB may approve a waiver or alteration of some or all of the consent requirements provided that:

1. "The research involves no more than minimal risk to the subjects"
2. "The waiver or alteration will not adversely affect the rights and welfare of the subjects"
3. "The research could not practicably be carried out without the waiver or alteration" and
4. "Whenever appropriate, the subjects will be provided with additional pertinent information after participation."

Documentation of Informed Consent

- Written consent form approved by the IRB and signed by the subject/subject's legally authorized representative may be either
    - Written consent document encompassing general requirements of informed consent described previously, or
    - A short form stating that the general requirements of informed consent (described previously) have been presented orally to the subject or the subject's legally authorized representative.

Waiver of Documentation

An IRB may waive documentation of consent if it finds either

- "That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality."
- "The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context."

EPA's codification of the Common Rule EXIT Disclaimer

Important Milestones in the Development of Codes of Research Ethics

Additional Protections in DHHS Regulation 45 CFR 46 beyond those in the Common Rule for Research Subjects Drawn from Vulnerable Populations, and Relation to EPA Regulation 40 CFR 26

Subpart B:

- **DHHS Regulations**: IRBs must apply additional criteria for research with pregnant women, fetuses, or newborns with uncertain viability to ensure that risks have been minimized and that any such research provides direct benefit to the subjects that outweighs the risks.
- **EPA Regulations**:
  - Defines intentional exposure research as the study of a substance in which the exposure to the subject would not have occurred but for the research.
  - Prohibits all intentional exposure research conducted/supported by EPA or submitted to EPA under the pesticide laws in pregnant women, their fetuses, nursing women, and children.

Subpart C:

- **DHHS Regulations:**
  - Establishes rules for research involving prisoners.
  - Requires that a majority of the members of IRBs reviewing proposed research with prisoners must not be associated in any way with the prison, and must include at least one member who is a prisoner or prisoner representative.
  - Prohibits research with prisoners except when it directly investigates criminal behavior or prisons, or directly benefits the subject prisoners. It sets additional requirements for the informed consent process to ensure that subject selection and consent is free from any duress or undue influence.
- **EPA Regulations:**
  - No special protections for prisoners in the EPA Final Human Studies Rule.
  - Subpart C provides special protections for pregnant women and fetuses who are involved in observational research conducted or supported by EPA. Research with these subjects can only occur if there is direct benefit to the woman or the fetus, or, in the absence of direct benefit, the risk is no greater than minimal and the research is

important for biomedical knowledge which cannot be obtained in any other manner.

- EPA's Subpart C is analogous to Subpart B of the DHHS regulations.

Subpart D:

- **DHHS Regulations:**
  - Establishes rules for research that involves children
  - Research can be conducted in children when there is no more than minimal risk. When there is greater than minimal risk, research can be conducted if there is a direct benefit to the child. If there is no direct benefit, research may only be conducted under special circumstances.
  - Informed consent should be obtained from the parents (or guardians) as well as the child, if capable based on age, maturity, and psychological state.
- **EPA Regulations:**
  - Establishes rules for research that involves observational studies of children.
  - Observational research (any research that is not intentional exposure research) can be conducted on children as long as it involves no more than minimal risk. Research that involves greater than minimal risk can only be conducted when there is direct benefit to the subject. Unlike in the DHHS rule, there is no provision in the EPA rule for the conduct of research when there is greater than minimal risk and no direct benefit to the child.
  - Informed consent should be obtained from the parents (or guardians) as well as the child, if capable based on age, maturity, and psychological state.

Federal Advisory Committee Act

- As a Federal advisory committee, the HSRB operates in accordance with the Federal Advisory Committee Act (FACA) 5 U.S.C. App.2 § 9.
- FACA was enacted in 1972 to govern the establishment, management, and termination of advisory committees within the executive branch of the Federal government. It ensures that federal advisory committees are accountable to the public by maximizing public access to advisory committee deliberations and minimizing the influence of special interests through balanced committee membership. In addition, the Act seeks to reduce wasteful expenditures and improve the overall administration of advisory committees.
- FACA ensures that federal advisory committees are:
  - Balanced in points of view represented for the function to be performed.
  - Governed by uniform procedures.
  - Limited to providing advice to the Agency.
  - Open to public scrutiny.
  - Terminated when no longer needed.

Federal Advisory Committee Act (PDF) (9 pp, 21K, About PDF)

EPA's FACA Fact Sheet (PDF) (2 pp, 54K, About PDF)

HSRB Membership

Board Composition

- Nationally recognized experts in relevant scientific or technical disciplines such as biostatistics, human toxicology, bioethics, and human health risk assessment.
- HSRB members may be selected from the environmental scientific/ technical fields, human health care professionals, academia, industry, public and private research institutes or organizations, other governmental agencies, or other relevant interest areas.
- Provide independent advice as either Special Government Employees or Regular Government Employees.

Membership Appointment Process

- Approximately six months before the expiration of a member's term, the new membership process begins.
- Process may include, but is not limited to
  - Querying the current expiring member concerning his/her continued interest in serving on the Board.
  - Agency discussion of whether new expertise or disciplinary perspective is required.
  - Publication of a Federal Register notice seeking nominations of qualified individuals to serve on the Board.
- If a Federal Register notice is published, EPA
  - Reviews the nominations resulting from the notice and other sources and publishes for public comment a Short List of final nominees.
  - Short List nominees who are not selected to serve as Board members may be considered for HSRB membership as vacancies arise or for service as a consultant to the HSRB.

Membership Appointment Process (continued)

- Factors considered for membership may include, but are not limited to:
  - Candidates' areas of expertise and professional qualifications.
  - Availability to participate in the Board's scheduled meetings.
  - Absence of any conflicts of interest and absence of an appearance of a lack of impartiality.
  - Independence with respect to the matters likely to come under HSRB review.
  - The overall balance of technical perspectives of the committee
  - Comments submitted on the Short List
- Selection of candidates
  - Numerous qualified candidates are likely to be identified.
  - Selection decisions involve careful weighing of many factors.
- HSRB members are appointed by the EPA Deputy Administrator, in consultation with the HSRB Designated Federal Officer (DFO).
- Members serve terms of up to three years under a system of staggered term of appointments.
- Agency policy is that advisory committee members should not serve more than six consecutive years.

HSRB Member Responsibilities

- Attend and participate in all Board meetings.
- Review extensive background materials between meetings.
- Prepare draft responses to Agency charge questions.
- Participate in developing consensus recommendations for the Agency.
- Prepare HSRB reports and recommendations.
- Abide by federal ethics regulations and statutes.

HSRB Leadership

HSRB is led by a Chair and Vice Chair

- Chair
  - Manages Board meetings and certifies the accuracy of Board meeting minutes.
  - Works with the DFO to develop meeting agendas.
  - Acts as Board liaison to the Agency.
- Vice Chair
  - Serves as Chair of the Board in the absence of the Board Chair.

HSRB Consultants

- Serve either as Special Government Employees or Regular Government Employees.
- Selected by the EPA Science Advisor, in consultation with the Board Chair and DFO.
- Attend specific Board or Subcommittee meetings and provide input and advice to the Board as requested.
- Provide specialized information or assistance to the Board, as needed.
- Are not HSRB members and do not participate in the Board's decision-making process.

Subcommittees

- EPA, or the HSRB with EPA's approval, may form subcommittees in accordance with the HSRB Charter.
- Subcommittee members need not be members of the Board.
- Subcommittees are expected to include at least one HSRB member, but may not include more than one-half of the HSRB members.
- Report their recommendations to the full committee; do not provide advice directly to EPA.

Workgroups

- A subset of committee or subcommittee members.
- May analyze relevant issues and facts.
- Undertake work on a specific task on behalf of the Board such as consult on meeting agendas or draft proposals.
- May conduct research.
- Provide input to the Board or a subcommittee; do not provide advice or recommendations directly to EPA.

Designated Federal Officer (DFO)

FACA requirements:

- Attending HSRB meetings
- Approving meeting agendas
- Adjourning of meetings when it is in the public interest to do so

Other responsibilities include:

- Providing general oversight of the HSRB to ensure full compliance with FACA.
- Serving as a liaison between the HSRB and EPA.
- Coordinating the public comment process.
- Preparing meeting minutes for certification by Chair.
- Coordinating the report writing process.
- Identifying and helping secure candidates for membership.
- Maintaining records of meetings and ensuring that records are publicly accessible.
- Maintaining records of costs and membership.
- Ensuring that members are familiar with their obligations under federal ethics regulations and conflict of interest statutes.

HSRB Meetings

- The HSRB holds approximately four public face-to-face meetings per year. In addition, the Board may have public teleconferences.
- Meetings are run according to an agenda, approved by the DFO, in consultation with the Agency and Board Chair.
- The meeting agenda and background materials are made available to the public and Board approximately two to four weeks before the meeting.
- Board members are assigned the role of Lead or Associate Discussant for one or more of the charge questions or topics to be considered at each meeting.
- Meetings are typically held in the Greater-Washington, DC area.

Meeting Format

- Open meeting.
- Identification of HSRB members (and consultants).
- Meeting administrative procedures by DFO.
- Introductory remarks by Chair and senior EPA officials.
- EPA follow-up on HSRB recommendations.
- Topic specific review
  - EPA presentation – EPA provides summary/background of topic(s) for Board consideration. Also provides opportunity for the Board to ask clarifying questions for further understanding.
  - Public comment – Generally, the public is invited to provide oral comments lasting no more than 5 minutes. The Board is provided the opportunity to ask clarifying questions of the public commenter.
  - Board discussants – A lead Board member presents a review of the topic and response to the presentations, followed by additional comments of associate Board member discussants.
  - Board discussion – Board members discuss the topic and respond to the Agency's charge, if applicable. Such remarks may also reflect upon public written or oral comments submitted at the meeting. If no charge question(s), general Board discussion on topic can occur.

Public Involvement

- Meetings are open to the public (unless closed as determined by the Administrator).
- Public access to all documents made available to or prepared by or for the committee.
- Opportunities for public comment, written and/or oral (as time permits), are provided at each meeting.

Meeting Minutes

- DFO prepares minutes for certification by the Chair.
- Draft copy of minutes is provided to Board to identify any errors.
- DFO makes certified copies available to the public within 90 days after the meeting.

Reports

- HSRB members prepare reports outlining their discussion and recommendations.
- Board Lead Discussants typically prepare the initial draft responses to the Agency's charge questions.
- Associate Discussant(s) work with the Lead Discussant to further refine the Board's response.
- All Board members are encouraged to respond to the Agency's charge, even if they are not Lead or Associate Discussants.
- HSRB recommendations reflect a consensus of the members. Each Board member has an opportunity to express his/her opinions and concerns as the Board works to achieve consensus on its recommendations. The Board's reports are agreed to by a consensus of its members.
- If consensus cannot be reached on a recommendation, the recommendation of the majority is presented to the Agency; minority views are included in the report at the request of the dissenting member(s).
- The Board, working with the DFO and Chair, edits the report for subsequent final Board review and approval at a public Board meeting.
- The Chair delivers approved Board reports or recommendations to the DFO, for subsequent transmission to the Administrator through the Science Advisor.

By-Laws

The HSRB prepared by-laws that serve as standard operating procedures for Board operations. The by-laws encompass eight articles as listed below:

Article I – Name
Article II – Authority
Article III – Mission and Scope
Article IV – Membership
Article V – Board Organization
Article VI – Meetings
Article VII – Reports and Recommendations
Article VIII – Amendments to By-Laws

The HSRB By-Laws (PDF) (6 pp, 33K, About PDF)

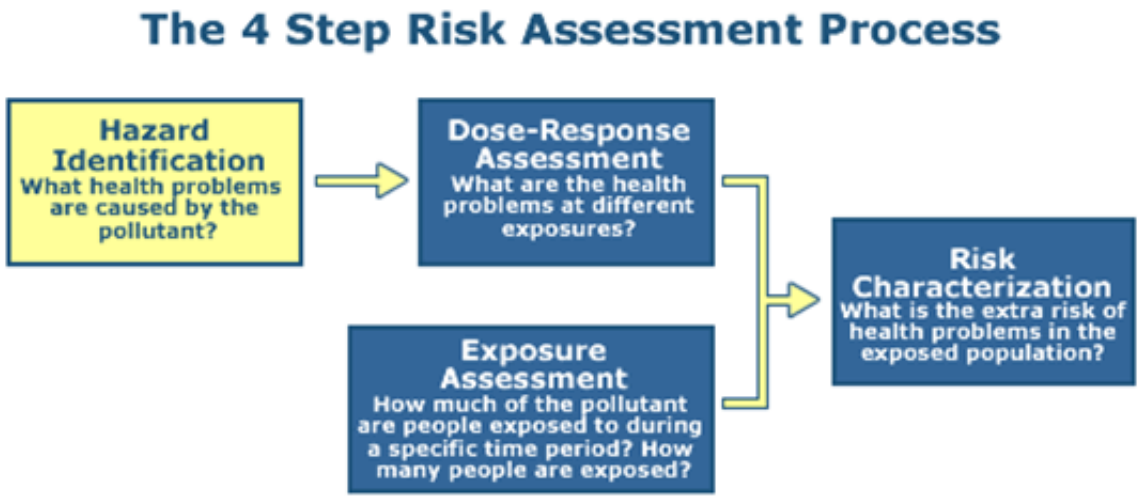
Risk Assessment

Risk Assessment

- A general understanding of the principles of risk assessment is useful in the consideration of research with human subjects.
- Risk assessment - the scientific process that characterizes the nature and magnitude of health risks to humans and ecological receptors from chemical contaminants and other stressors that may be present in the environment.
- Risk - the chance of harmful effects to human health or ecological systems resulting from exposure to a stressor.
- A stressor is any physical, chemical, or biological entity that can induce an adverse response.
- Risk is dependent on multiple factors:
  - How much of a stressor is present
  - Level of exposure a person has with the stressor
  - Inherent toxicity of the stressor

A four-step paradigm on risk assessment as outlined by the National Academy of Sciences.

Risk Assessment



The 1983 NAS report on risk assessment.

Risk Assessment

Risk, Hazard, and Exposure

- Risk = f (hazard and exposure)
- Hazard – a stressor that posses intrinsic toxic properties.
- Exposure - contact between an agent and a target; contact takes place at an exposure surface over an extended period.
- Sources of exposure:
  - Point source – a locatable and identifiable source
  - Nonpoint source – a diffuse source
  - Natural source
- Pathways of exposure
  - Air
  - Surface water
  - Ground water
  - Solid waste
  - Food
- Routes of exposure
  - Ingestion
  - Dermal
  - Inhalation

Risk Assessment

Endpoint

- Toxic effect upon which the risk assessment is based.
- Must be the most sensitive (most protective) for each population, and relevant to humans.

Dose Response Assessment and Endpoint Selection

- Lowest Observed Adverse Effect Level – lowest dose from a study at which adverse toxic effects are observed.
- No Observed Adverse Effects Level – the dose below the LOAEL at which no adverse toxic effects are observed.
- Point of Departure – any dose level used to quantify risk.

Risk Assessment

Expressing Risk: % Population Adjusted Dose (%PAD)

Used to express risks in acute (aPAD) and chronic (cPAD) dietary assessments

$$PAD = \frac{\text{Point of Departure (e.g., NOAEL)}}{\text{Uncertainty Factors}}$$

$$\%PAD = \frac{\text{Exposure}}{\text{PAD}} \times 100$$

Uncertainty Factors:

- Intraspecies – variability among humans
- Interspecies – extrapolating animal data to humans
- Extrapolating from less-than-lifetime to lifetime exposures
- LOAEL to NOAEL
- Incomplete data base
- increased concern for susceptibility of infants and children not addressed by other safety factors

Risk Assessment

Expressing Risk: Margin of Exposure (MOE)

Used to express risk for occupational/residential exposure assessments

$$\text{MOE} = \frac{\text{Point of Departure (e.g., NOAEL)}}{\text{Exposure}}$$

Risk Assessment

Expressing Risk: RfD/PAD vs. MOE

RfD / PAD

$$\text{Risk} = \frac{\text{exposure}}{\text{PoD}}$$

As exposure increases: %RfD or %PAD increases

MOE

$$\text{Risk} = \frac{\text{PoD}}{\text{Exposure}}$$

As exposure increases: MOE decreases

Risk Management/Characterization

- Process that evaluates how to protect human health.
- The purpose of risk assessment is to inform risk management decisions that compare regulatory options and select the optimal regulatory response for safety from the hazard.

More Information

More Information

Please click on the links below if you would like more information on the types of pesticide studies commonly seen by the HSRB.

- Background for application exposure monitoring test guidelines (PDF) (39 pp, 104KB,About PDF)
- Dermal exposure-outdoor (PDF) (14 pp, 37KB,About PDF)
- Dermal exposure-indoor (PDF) (14 pp, 37KB,About PDF)
- Inhalation exposure-outdoor (PDF) (13 pp, 35KB,About PDF)
- Inhalation exposure-indoor (PDF) (13 pp, 35KB,About PDF)
- Biological monitoring (PDF) (5 pp, 12KB,About PDF)
- Application exposure monitoring data reporting (PDF) (6 pp, 15KB,About PDF)

Confidential Financial Disclosure Form and Ethics Training

- Members and consultants of the HSRB are subject to Executive Branch financial disclosure requirements.
- Financial disclosure reports seek information regarding the candidate's financial interests, employment, holdings of stocks and bonds, and where applicable, sources of research support.
- Candidates from outside the federal government must submit a Confidential Financial Disclosure Form for Special Government Employees Serving on Federal Advisory Committees at the U.S. Environmental Protection Agency (EPA Form 3110-48 [5-02]).
- Candidates from within the federal government must submit either the OGE Form 450 or the SF-278, depending on their type of appointment in their home agency or department.
- The OGE-450 and the 3110-48 are confidential and cannot be disclosed to the public. The SF-278 is public and can be released to the public in accordance with established regulations.
- EPA will determine whether any financial conflicts of interest or appearances of a lack of impartiality may arise with respect to a candidate for the HSRB or for any member or consultant as the Board conducts its meetings.
- All HSRB members and consultants are required to take annual ethics training.
- EPA provides a computer-based ethics training to fulfill ethics training requirements.

EPA Form 3110-48(5-20) (PDF) (15 pp, 361K, About PDF)

OGE Form 450 (PDF) (7 pp, 205K, About PDF)

Form SF 278 (PDF) (18 pp, 247K, About PDF)

HSRB Ethics Training Program

Travel and Expense Reimbursement

- All members are eligible for reimbursement of their travel expenses (subject to the rules and restrictions of each participant's primary employer).
- Most members will be eligible for compensation for the time they spend preparing for and attending the meeting and for assisting with the preparation of the Board's report after the meeting.
- If you are eligible for compensation for your time, please remember to keep track of the time you devote to this activity.
- Lu-Ann Kleibacker or an Agency contractor will contact you concerning your travel arrangements. Please note that all travel arrangements must be made through our Agency travel office.

Timesheet for recording your work hours (PDF) (4 pp, 30K, About PDF)

Travel and expense reimbursement Frequently Asked Questions (PDF) (3 pp, 24K, About PDF)

Conclusions

On behalf of the U.S. Environmental Protection Agency, I thank you for taking the time to review this HSRB orientation program. I hope that you found the information it presented valuable as part of upcoming or continued service on the Board.

The Agency appreciates your service as a member of the HSRB, providing critical peer review advice on complex studies and policies addressing research with human subjects. Your participation on the Board strengthens the Agency's program in human research protections. I welcome any question or comments you may have about the HSRB.

Sincerely,

Warren Lux, M.D.
Director, Program in Human Research Ethics
Office of the Science Advisor