Workshop on Scientific Methods for Evaluating Endocrine Disruptor Screening Program Data and Estimating Dose-Response

Sponsored by
the Society for Risk Analysis and
Regulatory Checkbook

December 6, 2009

REGULATORY CHECKBOOK

AGENDA: AM SESSION

Time	Topic	Discussion Leader
0800	Food Quality and Protection Act Paperwork Reduction Act	Rick Belzer
0830	Theories of Validity in Science	Steve Lewis
0845	Sensitivity, Selectivity, Variability and Uncertainty in Tier 1 Assays	Sue Marty
0930	Using Tier 1 Data to Rank Chemicals for Endocrine Effects in Humans	Tom Vidmar
1030	Applying "Value of Information" (VOI) Principles to Tier 1 Test Data and "Other Scientifically Relevant Information"	Warner North
1100	Can Tier 1 Test Data Inform Priority-Setting for Human Health Risk Assessment?	Ray Witorsch
1145	Discussion and Collaboration	

AGENDA: PM SESSION

Time	Topic	Discussion Leader
1300	Information Quality Act and Risk Assessment	Rick Belzer
1330	Innovative Methods for Assessing Human Health Risks from Endocrine-Active Chemicals	Harvey Clewell
1415		Chris Borgert
1500		Bob Golden
1545	Discussants	Ray Witorsch Resha Putzrath
1630	Summing Up/Next Steps	Rick Belzer

AM Session

FOOD QUALITY PROTECTION ACT

21 USC 346a(p)(1)

Not later than 2 years after August 3, 1996, the Administrator shall in consultation with the Secretary of Health and Human Services develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate.

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PAPERWORK REDUCTION ACT

Public Protection Provision
5 CFR 1320.6

a) Notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information that is subject to the requirements of this part if:

1. The collection of information does not display … a currently valid OMB control number assigned by the Director in accordance with the Act…

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Agency Obligations under 5 CFR 1320.5(d)

1. To obtain OMB approval of a collection of information, an agency shall demonstrate that it has taken every reasonable step to ensure that the proposed collection of information:
    i. Is the least burdensome necessary for the proper performance of the agency's functions to comply with legal requirements and achieve program objectives;
    ii. Is not duplicative of information otherwise accessible to the agency; and
    iii. Has practical utility.

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What is 'Practical Utility'?

Practical utility means the actual, not merely the theoretical or potential, usefulness of information to or for an agency, taking into account its accuracy, validity, adequacy, and reliability, and the agency's ability to process the information it collects

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Reconciling these Laws

- EPA may require testing…

- …provided that the tests have been validated
- …provided that the information obtained is not duplicative
- …provided that the tests have practical utility
- … provided that it has a credible plan to use the data for a bona fide statutory purpose

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OMB's Terms of Clearance

- Promote and encourage the submission of other scientifically relevant information in lieu of all or some Tier 1 assays.
- Accept OSRI to the greatest extent possible.

Workshop Charge

- Devise a scheme that:
  - Adheres to OMB's Terms of Clearance
  - Fulfills the FQPA directive, using
    - …validated test systems and
    - …other scientifically relevant information
  - Substances
    - 'may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen,' or by implication
    - 'may not' have such an effect

Exercising Policy Discretion

- Statutory determinations are ruled by science, except for the definition of 'may'– as in 'may have an effect…'
- Ways to define 'may':
  - Binning ('may' / 'may not')
  - Ranking (least to most)
    - Likely to have an effect?
    - Likely to have an *adverse* effect?
- To be scientific, bins or ranks must be
  - Grounded on *scientific* similarities and differences
  - Transparent ('show your work')
  - Reproducible (outcomes predicable and consistent)

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PM Session

INFORMATION QUALITY ACT AND ENDOCRINE RISK ASSESSMENT

‘Information’ Defined

- ‘Any communication or representation of knowledge such as facts or data, in any medium or form...’
- ‘Does not include opinions, where the agency’s presentation makes it clear that what is being offered is someone’s opinion rather than fact or the agency’s views.’

‘Government Information’ Defined

- ‘Information created, collected, processed, disseminated, or disposed of by or for the Federal Government.’

'Dissemination' Defined

- "Agency initiated or sponsored distribution of information to the public.'
- 'Does not include distribution limited to government employees or agency contractors or grantees; intra- or inter-agency use or sharing of government information; and responses to requests for agency records under the Freedom of Information Act, the Privacy Act, the Federal Advisory Committee Act or other similar law.'

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Key Information Quality Principles

- Procedural principles
  - Transparency and reproducibility
  - Effective pre-dissemination review to minimize error
- Substantive principles
  - Utility
  - Integrity
  - Objectivity

‘Transparency’ and ‘Reproducibility’ Defined

- ‘Transparency’
  - Not explicitly defined.
  - ‘Show your work.’
- ‘Reproducibility’
  - Must be ‘capable of being substantially reproduced, subject to an acceptable degree of imprecision.’
  - Qualified third party is assumed.

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Effective Pre-dissemination Review Is Required

- Peer review is the preferred tool.
- Problems with government peer review:
  - Structural limitations.
  - Limited expertise in information quality.
  - Information quality absent from the charge.
- Is government peer review *effective* for ensuring information quality?
  - Rebuttable presumption of quality.
  - Procedural and substantive grounds to rebut.

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'Utility' Defined

- 'The usefulness of the information to its intended users, including the public.'
- '[W]hen transparency of information is relevant for assessing the information's usefulness from the public's perspective, the agency must take care to ensure that transparency has been addressed in its review of the information.'

‘Integrity’ Defined

‘The security of information—protection of the information from unauthorized access or revision, to ensure that the information is not compromised through corruption or falsification.’

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‘Objectivity’ Defined

- Substantive objectivity
  - ‘Accurate, reliable, and unbiased’.
- Presentational objectivity
  - ‘Presented in an accurate, clear, complete, and unbiased manner’.

Information Quality and Endocrine Risk Assessment

- Transparency
  - 'Show your work.'
- Reproducibility
  - Beyond transparency to underlying data.
- Objectivity
  - Role of 'science policy judgment'.
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- Utility
  - For priority setting.
  - As an input in regulatory analysis.
  - To inform regulatory decision-making.

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PM Session

NEXT STEPS: FUTURE COLLABORATION & PUBLICATION

Strawman Decision Theoretic Model

1. Preliminary bin / rank using OSRI.
2. Identify knowledge gaps.
3. Would filling a gap change bin /rank?
   a) If 'no,' stop; no practical utility.
   b) If 'yes,' proceed.
4. Does a Tier 1 assay fill such a gap?
   a) If 'no,' stop; no practical utility.
   b) If 'yes,' proceed.

Strawman Risk Assessment Framework

- Identify effect types of (dis?)interest.
- Identify effect magnitudes of (dis?)interest.

Future Collaboration

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