Webinar on the OHAT Approach for Systematic Review

Office of Health Assessment and Translation
National Institute of Environmental Health Sciences

September 26, 2013
Format and Logistics

• Brief OHAT staff presentation on a topic or theme

• Question and answer session on that topic
  – Use “Raise Hand” function if you would like to ask a question
  – Participants will be called upon in the order questions are received and phone line will be unmuted
  – Participants can ask their question directly

• Topics and timing
  – 4 topics as listed in the agenda
  – Remaining time (~60 minutes) for additional discussion
Webinar on the OHAT Approach for Systematic Review

Andrew Rooney, Ph.D.
Office of Health Assessment and Translation
National Institute of Environmental Health Sciences

September 26, 2013
Goals

1) to gain additional clarity on issues raised in public comments and

2) to discuss NTP’s progress at working through the case studies to test the systematic review framework
Topics or Themes

• Evaluating study quality and utility

• Confidence ratings in a body of evidence, where do you start?

• Evidence integration

• Update on case studies and next steps

• Additional discussion or questions from participants
OHAT Approach to Evaluating Study Quality and Utility
Definitions: Study Quality and Utility

• **Reporting quality**
  How well was the study reported?

• **Internal validity or risk of bias**
  How credible are the findings based on design and conduct of the study?

• **Directness and applicability**
  How well does the study address the topic under review?
Steps in Draft OHAT Approach Where Study Quality and Utility are Considered

**Step 1:** Prepare topic

**Step 2:** Search for and select studies

**Step 3:** Extract data from studies

**Step 4:** Assess individual study quality

**Step 5:** Rate confidence in body of evidence

**Step 6:** Translate confidence ratings into level of evidence for health effect

**Step 7:** Integrate evidence to develop hazard identification conclusions
Study Quality and Utility are Assessed in Several Different Steps

• Eligibility criteria (STEPS 1 and 2)
  – Critical aspects of study design or limitations in applicability

• Internal validity or risk of bias (STEP 4)
  – Study design and conduct
  – Reporting quality: Non-reporting has negative impact on risk of bias and attempts will be made to follow up with study authors
  – Confounding

• Directness and applicability (STEP 5)
  – Route, timing and duration of exposure
  – Upstream indicators
  – Relevance of animal model for human health

• Questions?
Confidence Ratings in a Body of Evidence,
Where do You Start?
Definitions: Body of Evidence and Initial Confidence

• A confidence rating for a body of evidence is developed by considering its strengths and weaknesses

• What comprises a “body of evidence”?
  – Studies with data on the same or related outcomes as defined in the protocol

• What do we mean by “initial confidence”?
  – The starting point for a study or group of studies prior to examining strengths and weaknesses
Method for Rating Confidence in a Body of Evidence

<table>
<thead>
<tr>
<th>Initial Confidence by Key Features of Study Design</th>
<th>Factors Decreasing Confidence</th>
<th>Factors Increasing Confidence</th>
<th>Confidence in the Body of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (++++) 4 Features</td>
<td>Risk of Bias</td>
<td>Large Magnitude of Effect</td>
<td>High (++++)</td>
</tr>
<tr>
<td></td>
<td>Unexplained Inconsistency</td>
<td>Dose Response</td>
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</tr>
<tr>
<td>Moderate (+++) 3 Features</td>
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<tr>
<td></td>
<td>Imprecision</td>
<td>• Studies report an effect and residual confounding is toward null</td>
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</tr>
<tr>
<td>Low (++) 2 Features</td>
<td>Publication Bias</td>
<td>• Studies report no effect and residual confounding is away from null</td>
<td>Low (+)</td>
</tr>
<tr>
<td>Very Low (+) ≤1 Features</td>
<td></td>
<td>Consistency</td>
<td>Very Low (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Across animal models or species</td>
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<td></td>
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<td>• Across dissimilar populations</td>
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<td>• Across study design types</td>
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<tr>
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<td>Other</td>
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<td>• e.g., particularly rare outcomes</td>
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Initial Confidence in Body of Evidence

- Initial Confidence Based on Key Study Design Features
  - Controlled exposure
  - Exposure prior to outcome
  - Individual outcome data
  - Comparison group used

- This Method Stratifies Initial Confidence:
  - Focuses on design features not labels
  - Reflects importance of observational studies in environmental health assessments

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- Human controlled trial
- Experimental animal
- Case-control
- Cohort
- Cross-sectional
- Ecologic
- Case series
- Case report
Initial Confidence by Study Design Features

• Starting point for evaluating confidence in a collection of studies in same initial confidence category
• Evaluate as a group for the same outcome
• Questions?

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- Prospective Cohort: 3-features
- Retrospective Cohort: 3-features
- Case-Control: 3-features
Evidence Integration
Further Consideration of Hazard Identification

• Previous Hazard ID Categories
  – **Known** to be a hazard to humans
  – **Presumed** to be a hazard to humans
  – **Suspected** to be a hazard to humans
  – **Not classifiable or not identified** to be a hazard to humans

• Updated
  – “**Not classifiable**” separated from “**Not identified**”
Evidence Integration in Step 7 of draft OHAT Approach

Step 1: Prepare topic
Step 2: Search for and select studies
Step 3: Extract data from studies
Step 4: Assess individual study quality

Step 5: Rate confidence in body of evidence

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Step 6: Translate confidence ratings into level of evidence for health effect

Step 7: Integrate evidence to develop hazard identification conclusions

Level of Evidence for Human Studies
- High
- Moderate
- Low

Level of Evidence for Animal Studies
- High
- Moderate
- Low

“Known”
“Suspected”
“Presumed”
“Not classifiable”
Hazard Identification in Draft OHAT Approach

• STEP 6: Level of evidence for health effect (on an outcome basis) reflects
  – Confidence in association between exposure to the substance and outcome
  – The direction of the outcome (effect or no effect)

• STEP 7: Integrate evidence by combining evidence streams to develop hazard ID
  – **Known** to be a hazard to humans
  – **Presumed** to be a hazard to humans
  – **Suspected** to be a hazard to humans
  – **Not classifiable** to be a hazard to humans

Evidence of no health effect supports Hazard ID conclusion of
  • **Not identified** to be a hazard to humans

Questions?
Update on the Case Studies
Progress on Case Studies

- Case studies to evaluate OHAT Approach or “Framework”
  - PFOA / PFOS exposure and immunotoxicity
  - BPA exposure and obesity

- Developing template protocol as case studies progress

- Screening studies nearing completion
References identified through other sources *(in process)*

Identified through database searches *(n=5,534)*

Title-abstract screened for relevance and eligibility *(n=2,687)*

References excluded for criteria established in protocol *(n=2,372)*

# of full-text articles excluded for pre-established criteria, with reasons
- exposure *(n=32)*
- outcome *(n=37)*
- review *(n=74)*
- other *(n=58)*

for example:
- 1st screen = unclear, no abstract
- full text screen = not relevant

Full-text articles assessed for relevance and eligibility *(n= 315)*

Studies included for data extraction in step 3, and risk of bias assessment in step 4 *(n=114)*

Human studies

Animal studies

Other relevant data *(e.g., in vitro or mechanistic studies)*

BPA and Obesity

References after duplicate removal *(n=1,632)*

BPA and Obesity

Studies included for data extraction *(n=86)*
Plans for Case Studies

• Plan to post screening results in October 2013

• Data extraction started
  – Refinement of DRAGON software ongoing
  – Expect completion in December 2013

• Then “lessons learned” webinar
  – Expect to hold webinar in late Spring 2014
  – Goal is to discuss the OHAT Approach or Framework

• Questions?
Acknowledgements

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• NTP Board of Scientific Counselors

• NTP BSC Working Group
  – Lynn Goldman, Chair, Dean, School of Public Health and Health Services, George Washington U.
  – Reeder Sams, Vice-chair, Acting Deputy Director, NCEA/RTP Division, USEPA
  – Lisa Bero, Director, San Francisco Branch, United States Cochrane Center at UC San Francisco
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  – Lauren Zeise, Chief, Reproductive and Cancer Hazard Assessment Branch, OEHHA, California EPA

• Protocol Technical Advisors
Additional Discussion
or
Questions?