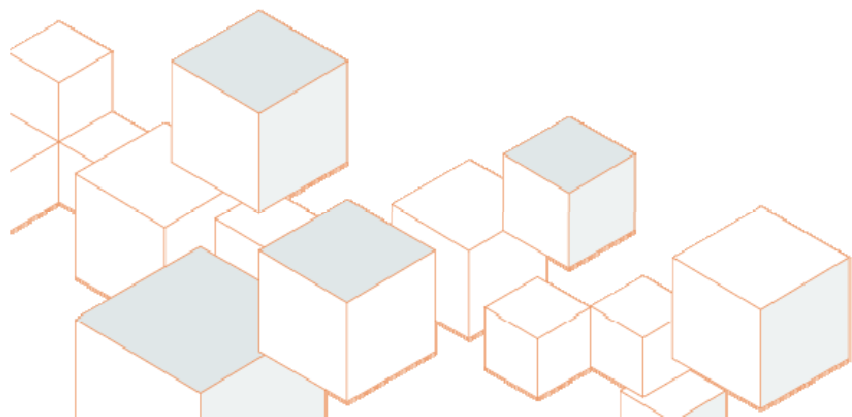


# Implementing the NRC Recommendations for EPA's IRIS Program

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Center for Advancing Risk Assessment Science and Policy (ARASP)  
September 19, 2014

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# ACC and the Center for Advancing Risk Assessment Science and Policy (ARASP)



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## ACC:

- Represents the leading companies engaged in the business of chemistry
- Committed to improved environmental, health and safety performance through Responsible Care<sup>®</sup>
- See: <http://americanchemistry.com/>

## ARASP:

- Coalition of 21 organizations focused on development and application of scientifically sound methods for conducting chemical assessments
- Promotes use of transparent and consistent approaches for data identification, integration and evaluation in chemical assessment
- See: <http://arasp.americanchemistry.com/>

# Improving Chemical Assessment



## Principles for Improving Chemical Hazard and Risk Assessment Programs



DESIGN



DATA



COMMUNICATION



REVIEW

1. Identify Key Issues
2. Utilize Data Over Defaults
3. Integrate Studies
4. Apply Consistent Criteria
5. Make Process Transparent
6. Characterize Hazards
7. Enhance Peer Review
8. Improve Accountability

Visit: <http://www.americanchemistry.com/Policy/Chemical-Safety/Chemical-Assessments/Principles.pdf>

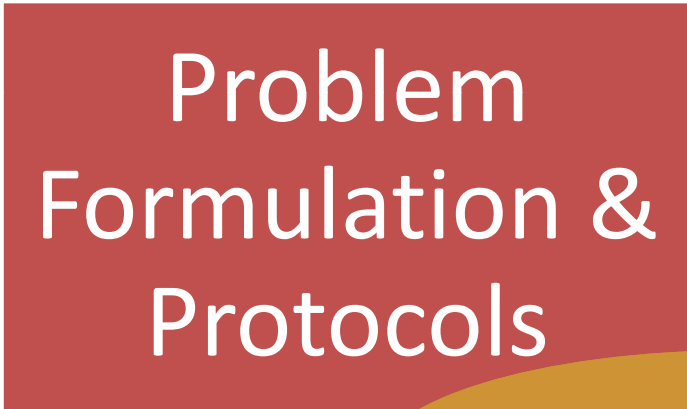
# NRC Recommendations for IRIS



## Process



Problem  
Formulation &  
Protocols



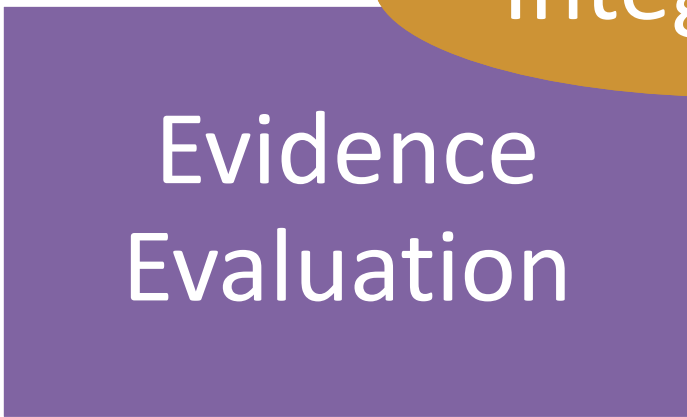
Evidence  
Identification



Integration



Evidence  
Evaluation

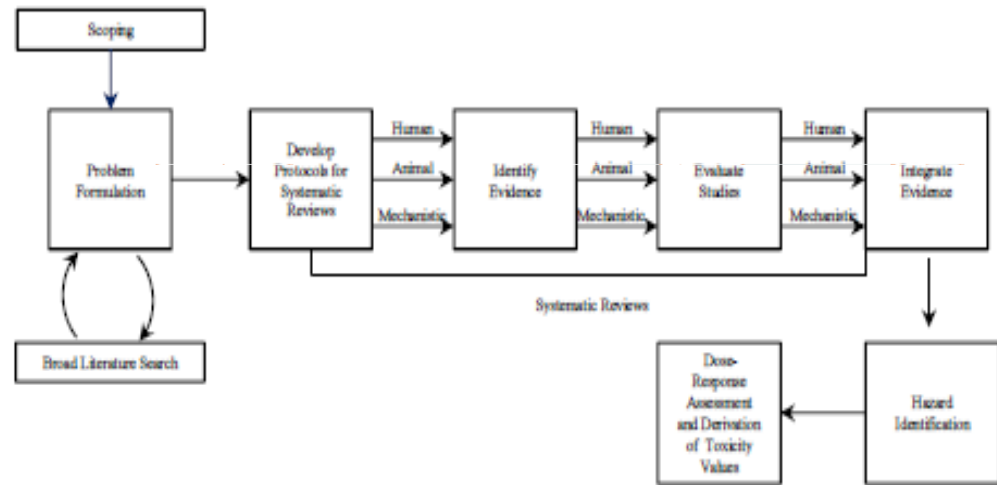


Toxicity Value  
Derivation



# PROCESS

\*denotes NAS high priority recommendations



## Transparent Methods

- Complete IRIS Handbook\*
- Develop guidance on process for nomination/reassessment
- Issue timeline for assessments in pipeline
- Provide schedule for implementation of the NRC recommendations, with milestones
- Conduct independent review of disposition of comments

# PROBLEM FORMULATION AND PROTOCOLS

\*denotes NAS high priority recommendations

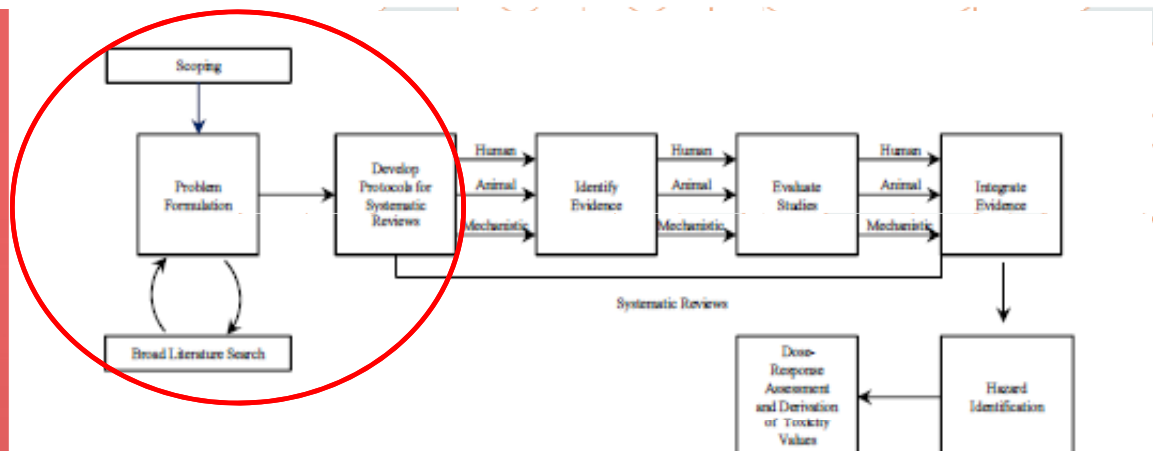


FIGURE S-1 Systematic review in the context of the IRIS process. The committee views public input and peer review as integral parts of the IRIS process, although they are not specifically noted in the figure.

## Asking the Right Questions

- ❑ Release protocols for all systematic reviews\*
  - ❖ Should include question to be addressed and specific methods used to address it\*
- ❑ Focus assessment on relevant exposure parameters (i.e. Does x cause y in humans exposed at dose z)
- ❑ Articulate the specific hypotheses to be evaluated in the assessment
  - ❖ Frame hypotheses with specific modes of action
  - ❖ Identify what methods will be employed to analyze the specific MOAs

# EVIDENCE IDENTIFICATION

\*denotes NAS high priority recommendations

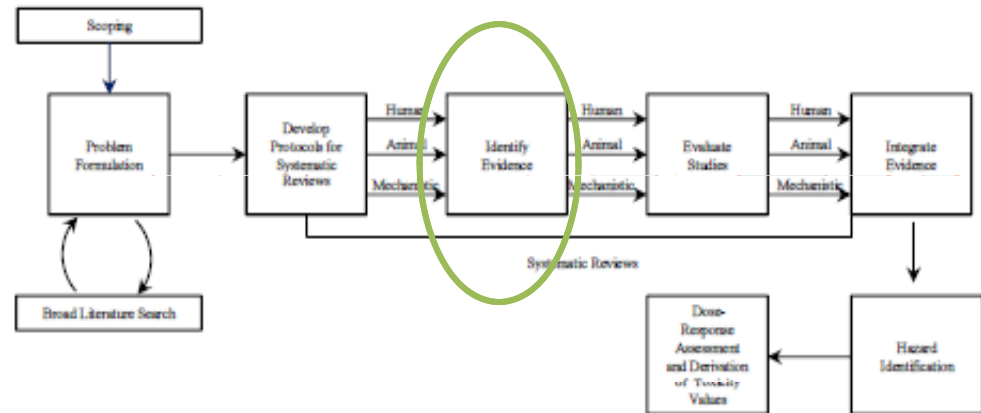


FIGURE S-1 Systematic review in the context of the IRIS process. The committee views public input and peer review as integral parts of the IRIS process, although they are not specifically noted in the figure.

## Identifying Relevant Studies

- ❑ Define the literature search strategy \*
  - ❖ Should include the date of the search, and publication dates searched and explicitly state the inclusion and exclusion criteria for studies\*
  - ❖ Should include a search strategy for each systematic review question\*
- ❑ Define process for consideration and evaluation of scientific information in association with the “IRIS Stopping Rules”

# EVIDENCE EVALUATION

\*denotes NAS high priority recommendations

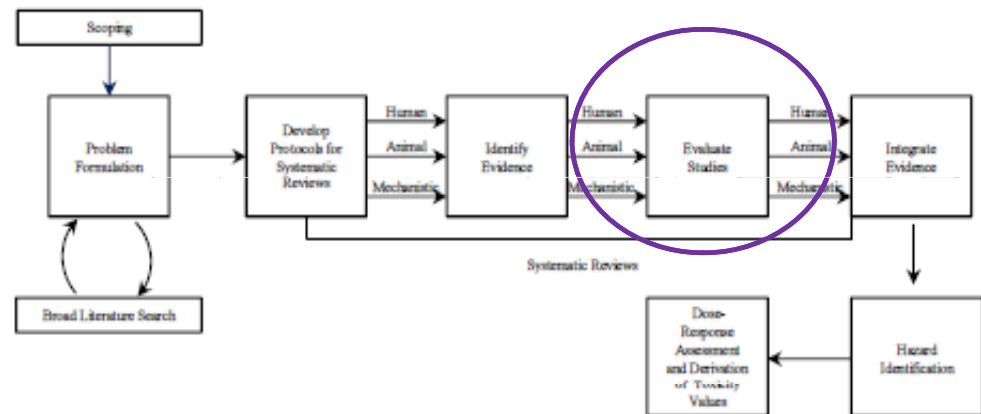


FIGURE S-1 Systematic review in the context of the IRIS process. The committee views public input and peer review as integral parts of the IRIS process, although they are not specifically noted in the figure.

## Evaluating Evidence Systematically

❑ Select transparent, reproducible, and scientifically defensible methods for evaluating individual studies\*

❖ Should identify study quality characteristics and how studies meet/do not meet criteria



# EVIDENCE INTEGRATION

\*denotes NAS high priority recommendations

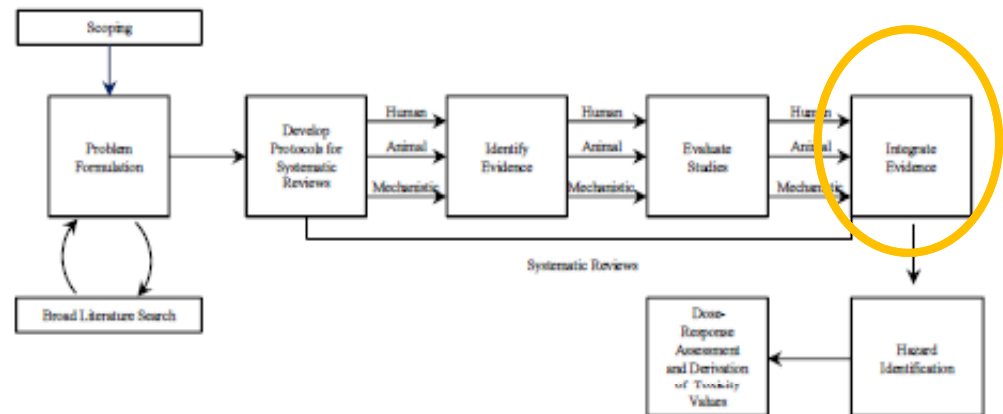


FIGURE S-1 Systematic review in the context of the IRIS process. The committee views public input and peer review as integral parts of the IRIS process, although they are not specifically noted in the figure.

## Integrating the Evidence

- Improve transparency and process for evidence-integration\*
  - ❖ Detail how the quality review and risk of bias evaluations inform the evidence integration process
- Develop the capacity to do Bayesian modeling\*
  - ❖ Incorporate MOA
  - ❖ Develop case study examples
- Integrate evidence using the alternative hypothesis approach

# TOXICITY VALUE DERIVATION

\*denotes NAS high priority  
recommendations

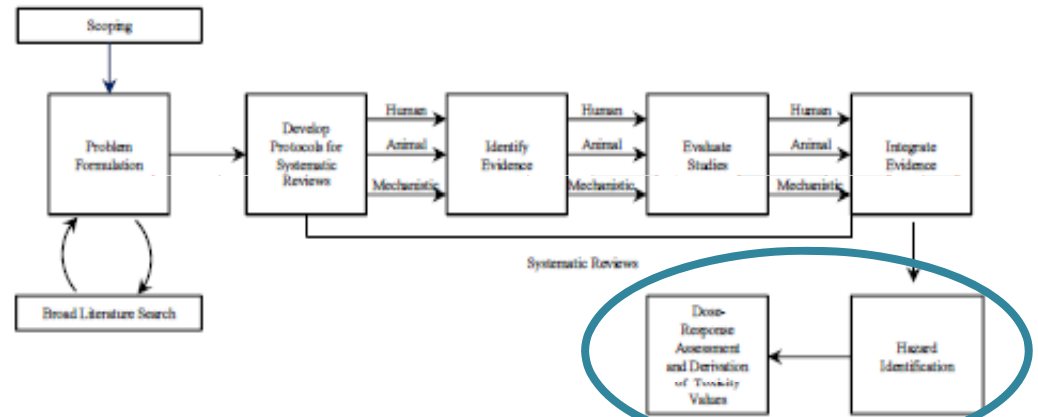


FIGURE S-1 Systematic review in the context of the IRIS process. The committee views public input and peer review as integral parts of the IRIS process, although they are not specifically noted in the figure.

## Useful Information for Risk Management

- ❑ Present two dose-response estimates: a central estimate and a lower-bound estimate\*
- ❑ Make uncertainty analysis an integral component of the IRIS process\*
- ❑ Conduct public peer review of proposed causality framework
- ❑ Present linear and non-linear models in the assessment and develop relevant risk estimates based on each model

## Short Term Next Steps

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- Provide a schedule for implementing NRC 2011 and 2014 recommendations
- Develop a protocol for each IRIS assessment in the pipeline
- Include a central estimate, for non-cancer and cancer in all assessments
- Release updated draft of the IRIS Handbook for public comment