



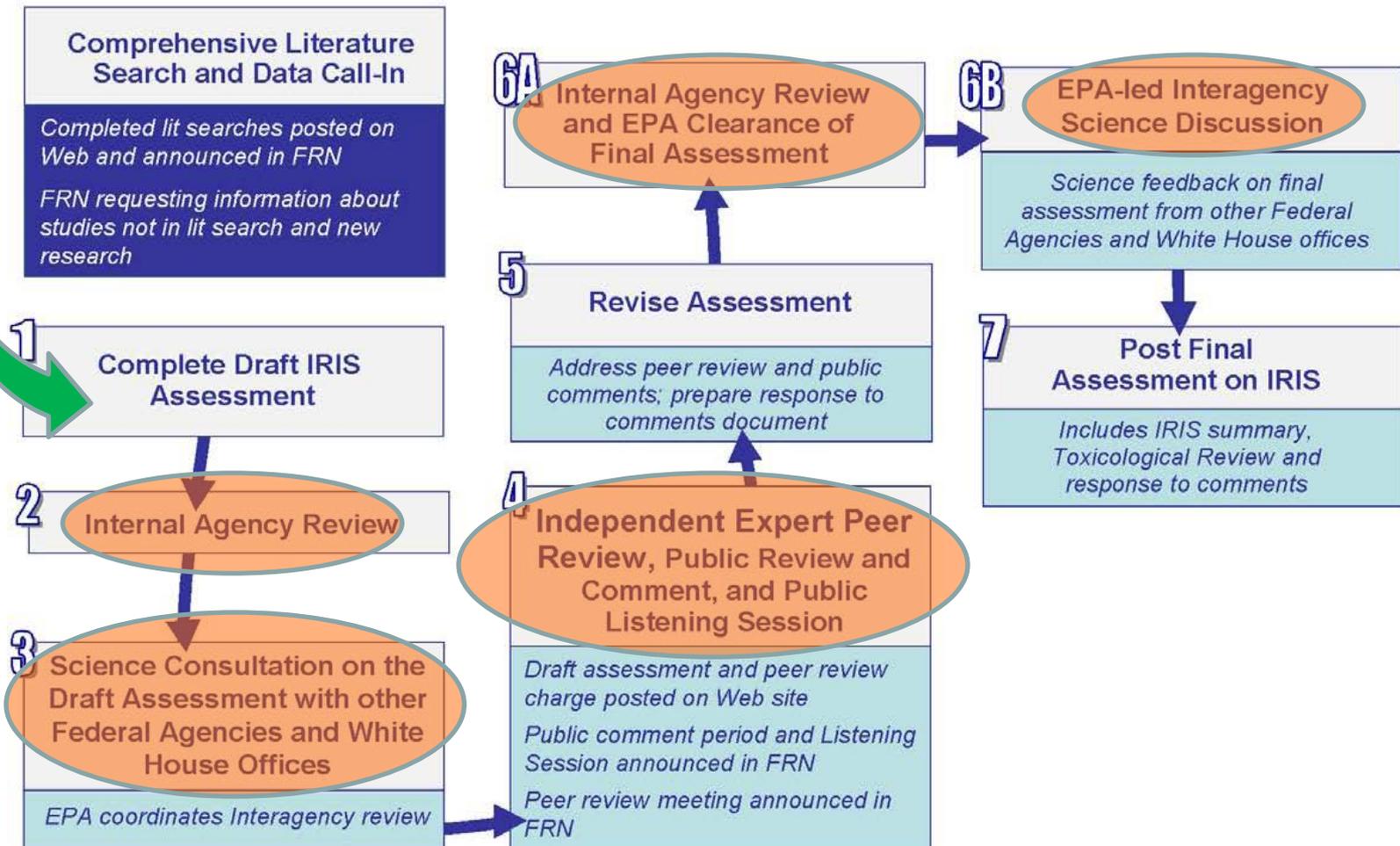
IRIS: Toxicological Reviews and Process

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IRIS Assessments Receive Multiple Reviews; NRC Focus on the First Step





Recommendations from the NAS (2011) Panel

- Recommendations for each of the 5 steps



- General guidance for the overall process:
 - Elaborate an overall, documented, and quality-controlled process for IRIS assessments.
 - Ensure standardization of review and evaluation approaches across the program.
 - Assess disciplinary structure of teams.

The NAS did not recommend that IRIS assessments be delayed while new approaches are implemented.



IRIS Is Adopting All Recommendations of the NAS (2011) Panel

Steps Outlined by NAS (2011)

1. Identify Evidence



2. Evaluate Evidence



3. Synthesize and Integrate Evidence



4. Select Studies to Derive Toxicity Values

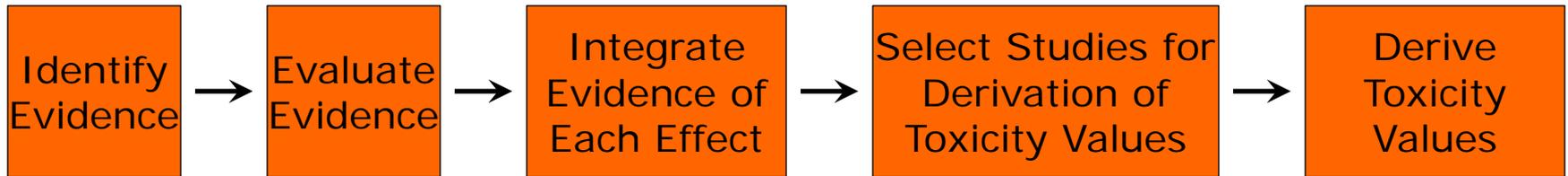


5. Derive Toxicity Values

- IRIS is improving assessments by adopting principles of systematic review.
- IRIS has implemented a QA process to ensure quality and consistency throughout the program.
- IRIS is improving its process through early public engagement.



A New Preamble Gives Guidance for Each Part



Source: Adapted from NRC (2011) Figure 2-1

Preamble to IRIS Toxicological Reviews

1. Scope of the IRIS Program
2. Process for Developing and Peer-Reviewing IRIS Assessments
3. Identifying and Selecting Pertinent Studies
4. Evaluating the Quality of Individual Studies
5. Integrating the Overall Evidence of Each Effect
6. Selecting Studies for Derivation of Toxicity Values
7. Deriving Toxicity Values



IRIS Assessments Consist of Multiple Systematic Reviews

- What health hazards are associated with Agent X?
 - What is the evidence of an association with cancer?
 - What is the evidence of an association with reproductive toxicity?
 - What is the evidence . . . (etc.)?
- What can we say about dose-response curves?

Two important differences from systematic reviews of medical interventions:

- ***Most evidence we have comes from animal bioassays and observational studies.***
- ***Our process is a very public one.***



IRIS Is Implementing an Overall, Documented, Quality-Controlled Process

- An interdisciplinary Assessment Team (AT) of scientists develops each assessment.
- Discipline-specific groups (e.g., PBPK, statistics) coordinate to ensure consistency across assessments and to solve cross-cutting issues.
- Major decisions are discussed by one of three *Chemical Assessment Support Teams* (CAST) chaired by senior NCEA science managers.
- These processes ensure the use of standardized approaches throughout IRIS and ensure that major science decisions are rigorously vetted.
- Key decisions are disseminated to promote consistent evaluation approaches across IRIS (CAST meeting notes, "Handbooks").



Improved Protocols Also Contribute to Improved IRIS Assessments

NAS (2011) Recommendation

Expanded description of methods

- Identifying and selecting studies
- Weight-of-evidence approaches

EPA Response

A Preamble to each IRIS assessment will discuss

- Identifying and selecting pertinent studies
- Evaluating the quality of individual studies
- Weighing the overall evidence of each effect
- Selecting studies for derivation of toxicity values
- Deriving toxicity values



Improved Protocols Also Contribute to Improved IRIS Assessments

- New Preamble (20 pages) distills 1600 pages of EPA risk assessment guidance.
- New draft “Handbook” on instructions and considerations involved in assessment development.
- New concise document structure with improved treatment of hazard ID and dose-response.
- *Science and Decisions*: R&D is focused on results that become part of an IRIS assessment:
 - Unified dose-response for all health effects.
 - Better treatment of uncertainty and variability.⁹



Old Versus New IRIS Documents

Old IRIS Document

- Introduction (1/2 page)
- Literature search (1 page)
- Lengthy study summary narratives (all studies, many pages, detailed descriptions)
- Combined section with hazard identification and dose-response

Standard Assessment: 300 pages
Complex Assessment: 1000 pages

New IRIS Document Structure in Response to 2011 NRC Recommendations

- Preamble (20 pages)
- Detailed literature search strategy
- Concise evidence tables of key studies (key studies only, succinct, tabular)
- Separate section for Hazard Identification
- Separate section for Dose Response Analysis

Standard Assessment: 100 pages
Complex Assessment: 200 pages



Summary of Improvements

Improved product

IRIS assessments are becoming more clear, more concise, more systematic.

Improved QA/QC

Senior science managers review IRIS assessments at critical time points and coordinate to ensure quality and consistency.

Implementation will continue to evolve as we receive peer review advice

Improved throughput

Please recognize the need for IRIS to complete more assessments in less time.



Summary of Improvements at Every Step

Steps Outlined by NAS (2011)

1. Identify Evidence

2. Evaluate Evidence

3. Synthesize and Integrate Evidence

4. Select Studies to Derive Toxicity Values

5. Derive Toxicity Values

- Protocols for systematic literature search
- Documentation of search/screening process

- Ongoing progress
- Multiple workshops

- Criteria for evaluating study quality
- Identification of studies of highest quality and pertinence

- Criteria for study selection
- Toxicity values for each effect
- Tools to facilitate consistent analyses