EPA
United States
Environmental Protection
Agency

Systematic Review for Chemical Assessments: Core Elements and Considerations for Rapid Response

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EPA's Computational Toxicology Communities of Practice

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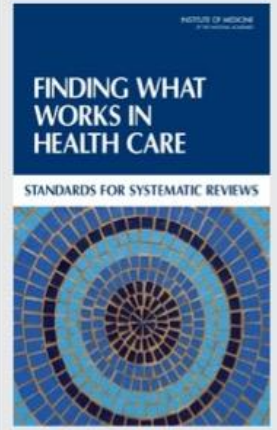
Systematic Review



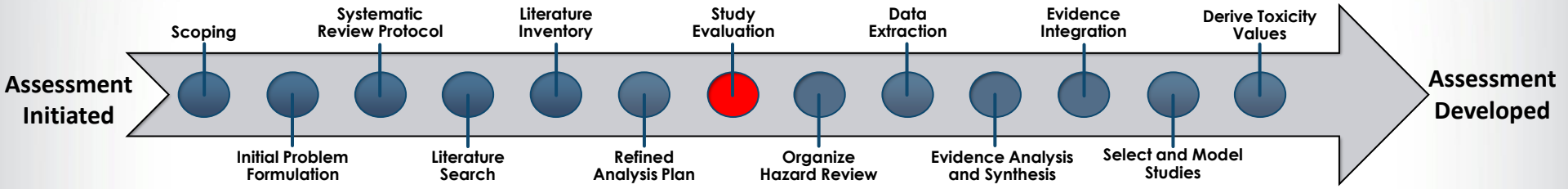
A structured and documented process for transparent literature review[1,2]

"… systematic review is a scientific investigation that focuses on a specific question and uses explicit, pre-specified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. The goal of systematic review methods is to ensure that the review is complete, unbiased, reproducible, and transparent"

[1] Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act. EPA-HQ-OPPT-2016-0654. https://www.epa.gov/sites/production/files/2017-06/documents/prepubcopy_tsca_riskeval_final_rule_2017-06-22.pdf

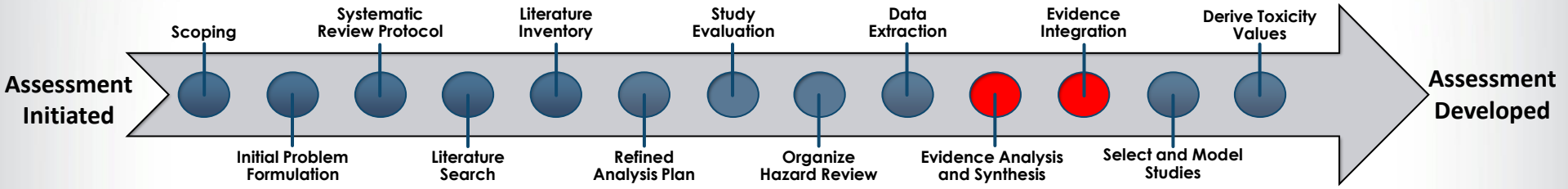
[2] Institute of Medicine. Finding What works in Health Care: Standards for Systematic Reviews. p.13-34. The National Academies Press. Washington, D.C. 2011

Individual Study Evaluation



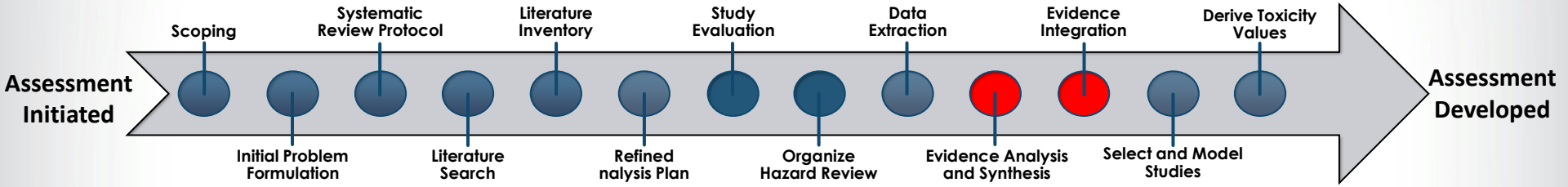
- General approach same for human and animal studies
- Evaluation process focused on:
  - Internal validity/bias
  - Sensitivity
  - Applicability (relevance to the question)
  - Reporting quality

Evidence Synthesis and Integration



- Synthesis of evidence is more than counting the number of "positive" and "negative" studies
- Consider the influence of bias and sensitivity when describing study results and synthesizing evidence
  - Synthesis should primarily be based on studies of medium and high confidence (when available)
- Use structured framework to aid in transparency

Moving from Synthesis to Integration



Step 1: Within Evidence Stream Judgements

- Results of Human Health Effect Study Synthesis
- Results of Animal Health Effect Study Synthesis
- Results of Synthesis of Mechanistic Evidence Informing the Human and Animal Syntheses

Step 2: Across Evidence Stream Integration

Certainty in the Evidence: How Confident in the Research

- Are the research studies well done? Risk of bias
- Are the results consistent across studies ? Inconsistency
- How directly do the results relate to the question? Indirectness
- Is the association precise - due to random error? Imprecision
- Are these all of the studies that have been conducted? Pub. Bias
- Is there anything else that makes us particularly certain? Large associations, worst case scenario predictors still allows strong conclusions, exposure-effect relation