

# Draft Development Materials for the Integrated Risk Information System (IRIS) Toxicological Review of Inorganic Arsenic (iAs)

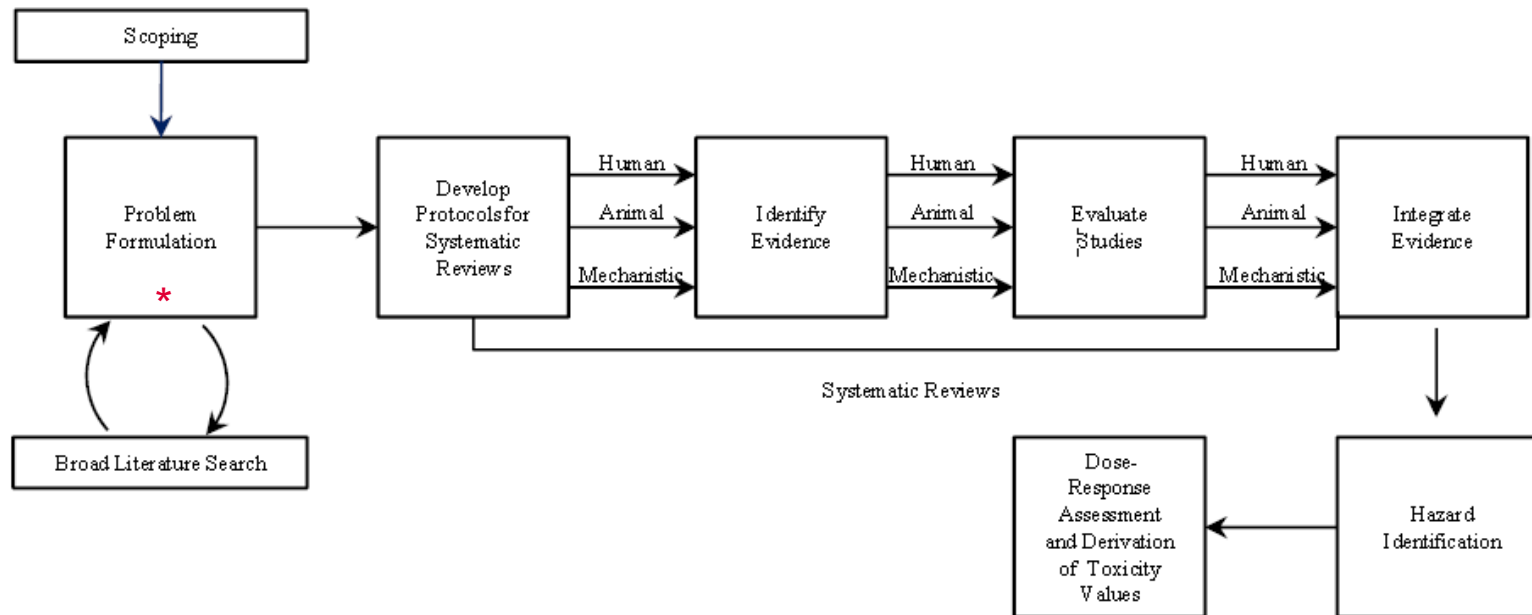
## Key Science Issue 1 – Structure and Utility of the Assessment Development Plan

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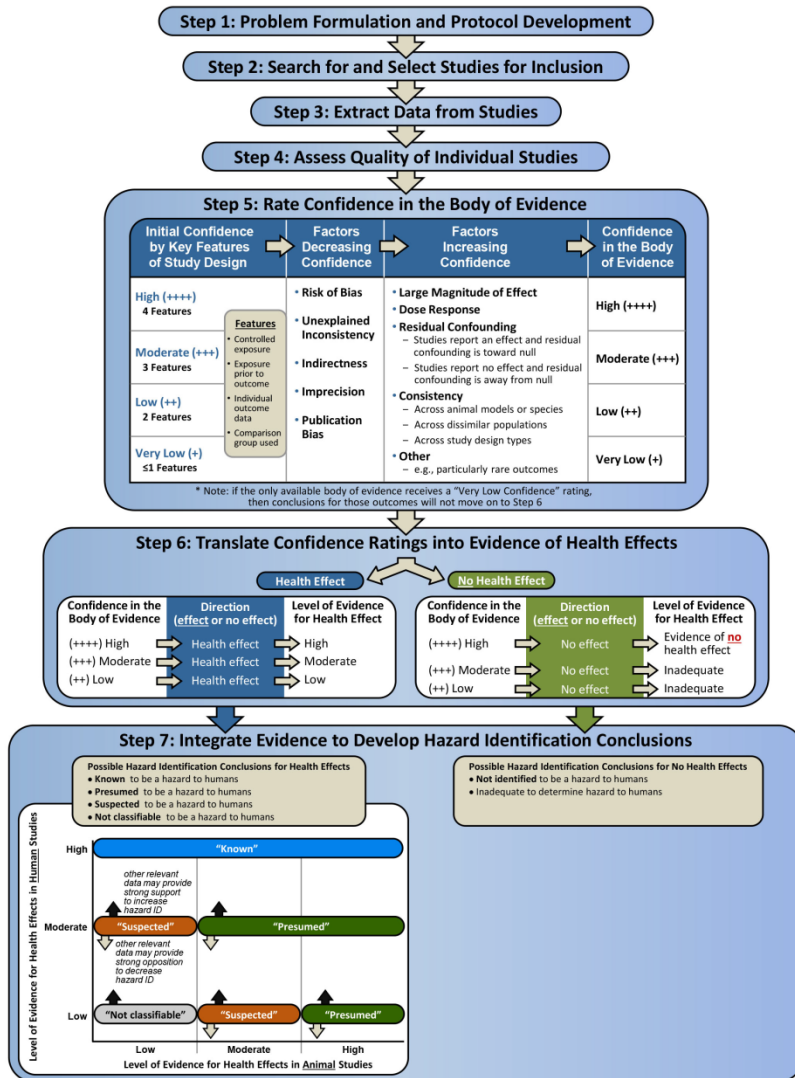
# NRC Framework for IRIS Assessment Development Process



- Scoping and broad literature search inform problem formulation
- Broad literature search sets up problem formulation: specific questions for which systematic review protocols are to be developed
- \* iAs draft materials establish elements of problem formulation prior to broad literature search

Source: National Research Council (NRC). 2014. *Review of EPA's Integrated Risk Information (IRIS) process*. Washington, DC: National Academies Press. Figure S-1

# The OHAT Approach for Systematic Review



IRIS iAs Draft Development Materials Framework for Causal Determination of Human Health Effect Endpoints

IRIS should develop same type of criteria and framework for **evidence integration**

Source: Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. Systematic Review and Evidence Integration for Literature-Based Environmental Health Science Assessments. Environ Health Perspect. Figure 1

# OHAT Evaluation of Confidence in the Body of Evidence and Relationship to Bradford Hill Considerations

Hill consideration	Relationship to the OHAT Approach
Strength	Considered in upgrading the confidence rating for the body of evidence for <b>large magnitude of effect</b> and downgrading the confidence rating for <b>imprecision</b> .
Consistency	Considered in upgrading confidence rating for the body of evidence for <b>consistency across study types, across dissimilar populations, or across animal species</b> ; and in integrating the body of evidence among human, animal, and other relevant data; also in downgrading confidence rating for the body of evidence for <b>unexplained inconsistency</b> .
Temporality	Considered in <b>initial confidence ratings</b> by key features of study design, for example experimental studies have an initial rating of “High Confidence” because of the increased confidence that the controlled exposure preceded outcome.
Biological gradient	Considered in upgrading the confidence rating for the body of evidence for evidence of a <b>dose-response</b> relationship.
Biological plausibility	Considered in examining non monotonic <b>dose-response</b> relationships and developing confidence rating conclusions across biologically related outcomes, particularly outcomes along a pathway to disease. Other relevant data that inform plausibility such as physiologically based pharmacokinetic and mechanistic studies are considered in integrating the body of evidence. Also considered in downgrading the confidence rating for the body of evidence for <b>indirectness</b> .
Experimental evidence	Considered in setting <b>initial confidence ratings</b> by key features of study design and downgrading the confidence rating for <b>risk of bias</b> .

“Aspects of an association that suggest causality are drawn from Hill” – IRIS iAs Draft Development Materials

Source: Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. Systematic Review and Evidence Integration for Literature-Based Environmental Health Science Assessments. Environ Health Perspect. Table 3