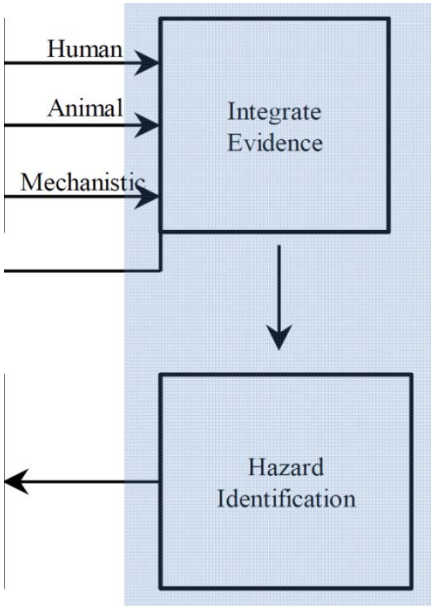
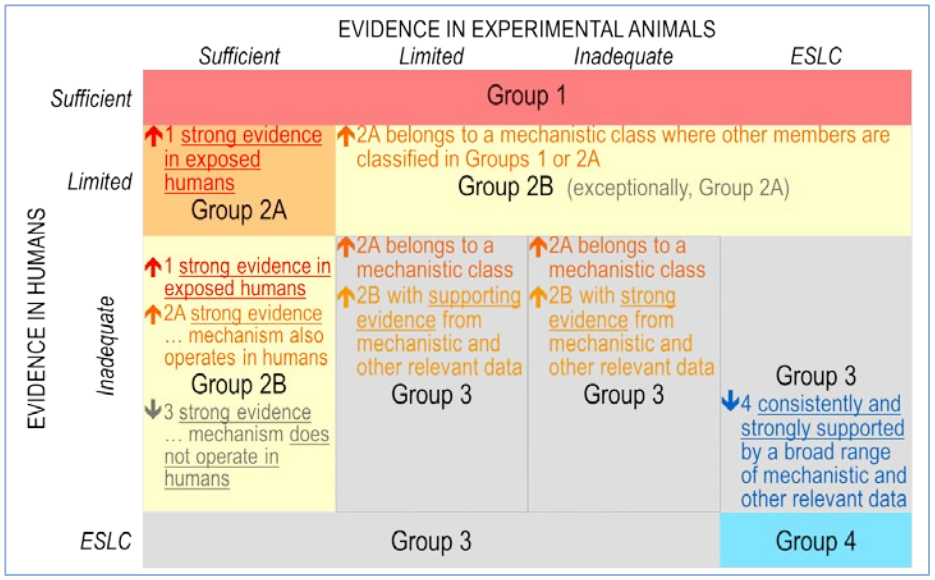
Integrating Evidence… It is not a novel challenge

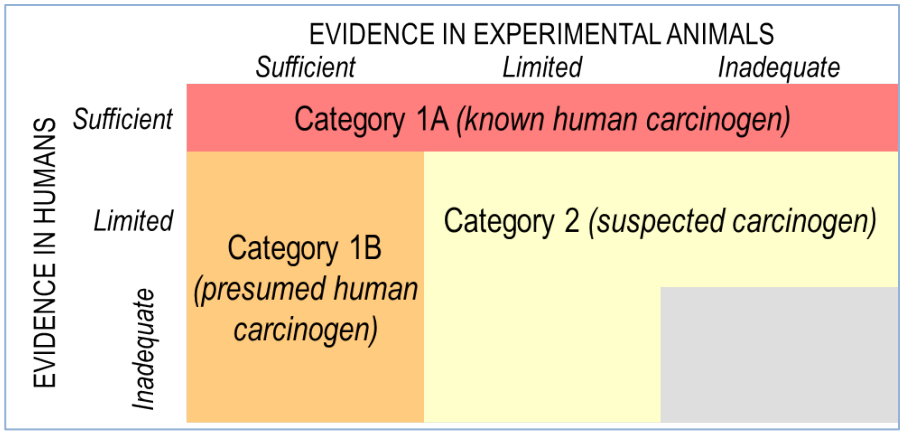
NRC, 2014



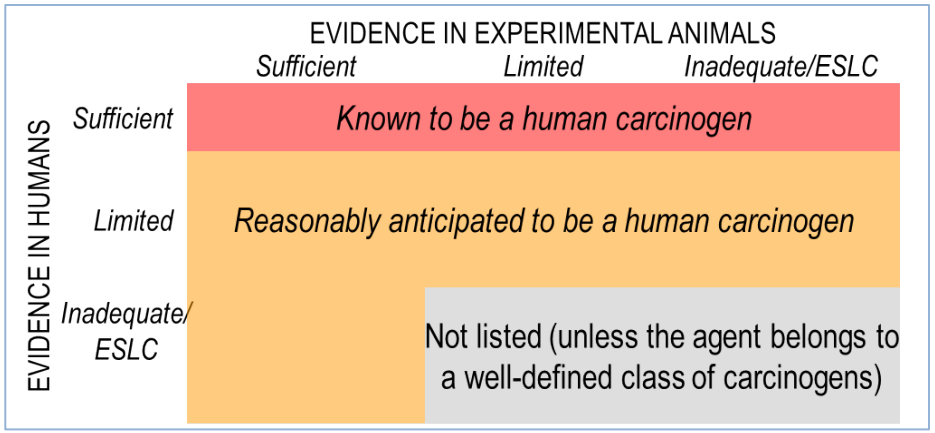
International Agency for Research on Cancer



Globally Harmonized System
of Classification and Labelling of Chemicals



National Toxicology Program
Report on Carcinogens



Most images courtesy of J. Vincent Cogliano (US EPA)

Integrating Evidence… What IS "evidence"?

NRC 2014 (Review of the Formaldehyde Assessment in the NTP 12th RoC):

> "The statement of task specifically asked the committee to "integrate the level-of-evidence conclusions, and considering all relevant information in accordance with the RoC listing criteria, make an independent listing recommendation for formaldehyde and provide scientific justification for its recommendation" (Appendix B). **The committee notes that the term *integrate* does not have a standard definition in the context of hazard assessment. The committee understood the term in its conventional sense of bringing together parts into a whole**."

Point #1: *"Not all evidence was created equal…"*

NRC 2014 (Review of the Formaldehyde Assessment in the NTP 12th RoC):

> "To be listed as "*reasonably anticipated as a human carcinogen*" or "*known to be a human carcinogen*", the RoC listing criteria only requires **information to be integrated across human studies** or **across animal studies**, and supporting information […] from mechanistic studies."

NRC 2014 (Review of the EPA IRIS process):

> "…the EPA guidelines for cancer risk assessment state that classification of a chemical as a human carcinogen is reached when there is "convincing epidemiologic evidence of a *causal* association between human exposure and cancer" (EPA 2005). According to the guidelines, the **determination can be made irrespective of the strength of the animal data**."

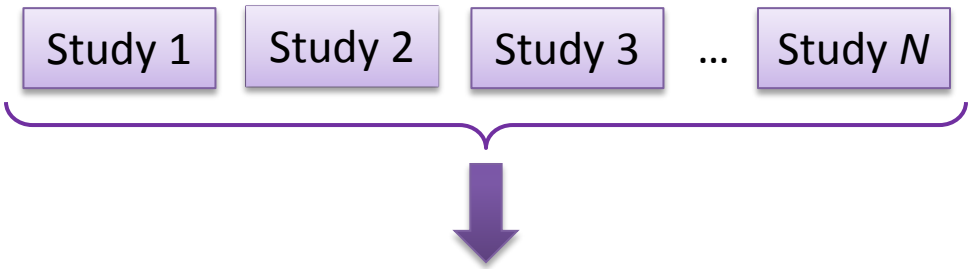
NRC 2014 (Review of the Formaldehyde Assessment in the NTP 12th RoC):

> "The committee notes that *evidence in experimental animals* and *a known mechanism of action* ***is not required*** by the RoC listing criteria in making a listing recommendation that a substance is known to be a human carcinogen if the evidence from studies in humans is sufficient and indicates an association between exposure and human cancer."

Integrating Evidence for Hazard Identification
…within each "data domain"

Point #2: ***We should not attempt to integrate ALL evidence***

Human or Animal Evidence



- ***Sufficient*** epidemiologic evidence of an association consistent with causation
- ***Suggestive*** epidemiologic evidence of an association consistent with causation
- ***Inadequate*** epidemiologic evidence to infer a causal association
- Epidemiologic evidence consistent with ***no causal association***

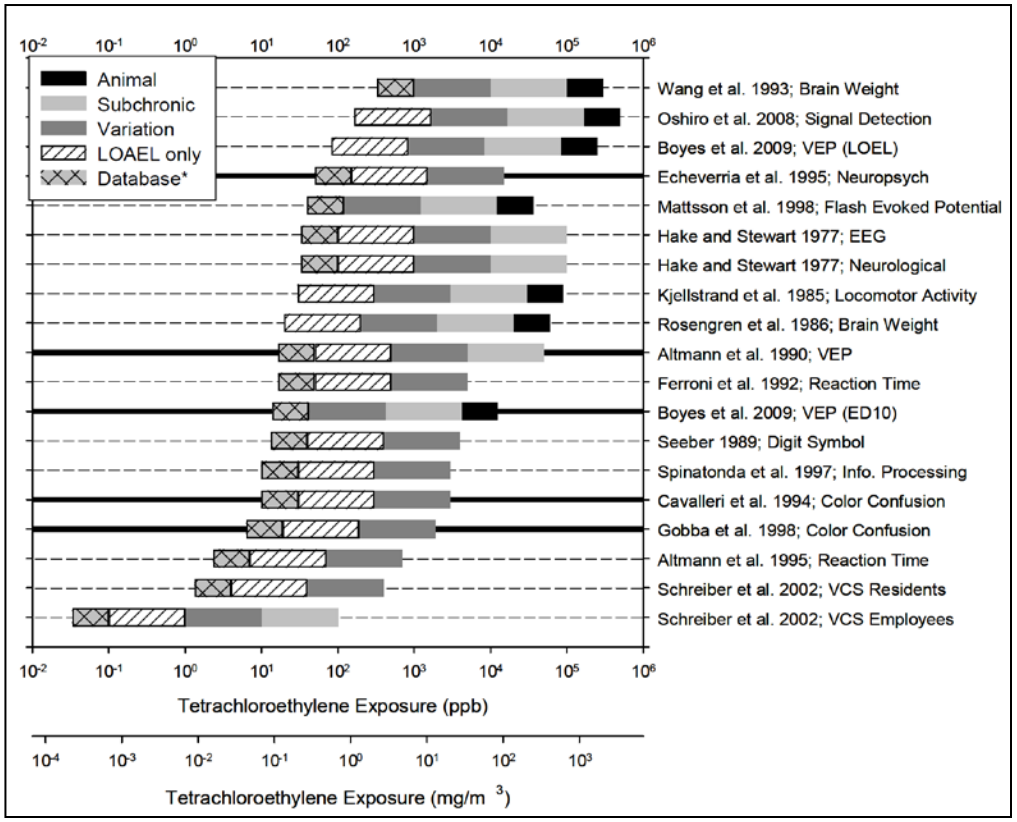
NRC 2014 (Review of the EPA IRIS process)

Point #3: ***It is more important to define how "sufficient," "suggestive," and "inadequate" terms are ascribed to the body of evidence within each "data domain"***

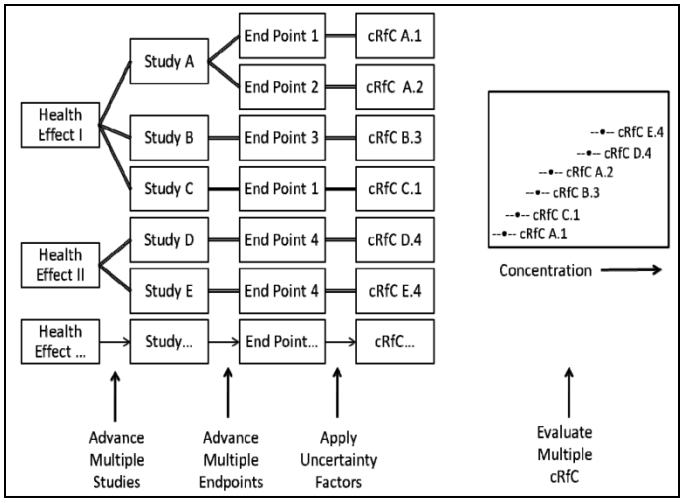
Integrating Evidence for Dose Response Assessment

Point #4: Evidence integration does not stop at "hazard identification"

NRC, 2010 and NRC, 2014



NRC, 2011



NRC, 2014