



Pathways to Implementation of the NRC Recommendations

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Summary of Recommendations for Integrating Evidence

1. Apply a consistent, systematic approach for evaluating each evidence stream separately
Human, non-human and mechanistic studies
2. Then integrate evidence
3. Build off existing methods for complete and transparent methodology for integrating evidence ***with a structured process:***
OHAT/ Navigation Guide/GRADE
Adjust for environmental health
4. Approach should harmonize cancer/noncancer

The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Integration of Animal and Human Evidence for PFOA Effects on Fetal Growth

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The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Human Evidence for PFOA Effects on Fetal Growth

Paula I. Johnson,¹ Patrice Sutton,¹ Dylan S. Atchley,¹ Erica Koustas,² Juleen Lam,² Saunak Sen,³ Karen A. Robinson,^{4,5,6} Daniel A. Axelrad,⁷ and Tracey J. Woodruff¹

The Navigation Guide—Evidence-Based Medicine Meets Environmental Health: Systematic Review of Nonhuman Evidence for PFOA Effects on Fetal Growth

Erica Koustas,¹ Juleen Lam,¹ Patrice Sutton,² Paula I. Johnson,² Dylan S. Atchley,² Saunak Sen,³ Karen A. Robinson,^{4,5,6} Daniel A. Axelrad,⁷ and Tracey J. Woodruff²

The Navigation Guide Systematic Review Methodology: A Rigorous and Transparent Method for Translating Environmental Health Science into Better Health Outcomes

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Systematic Review and Evidence Integration for Literature-Based Environmental Health Science Assessments

Andrew A. Rooney, Abee L. Boyles, Mary S. Wolfe, John R. Bucher, and Kristina A. Thayer



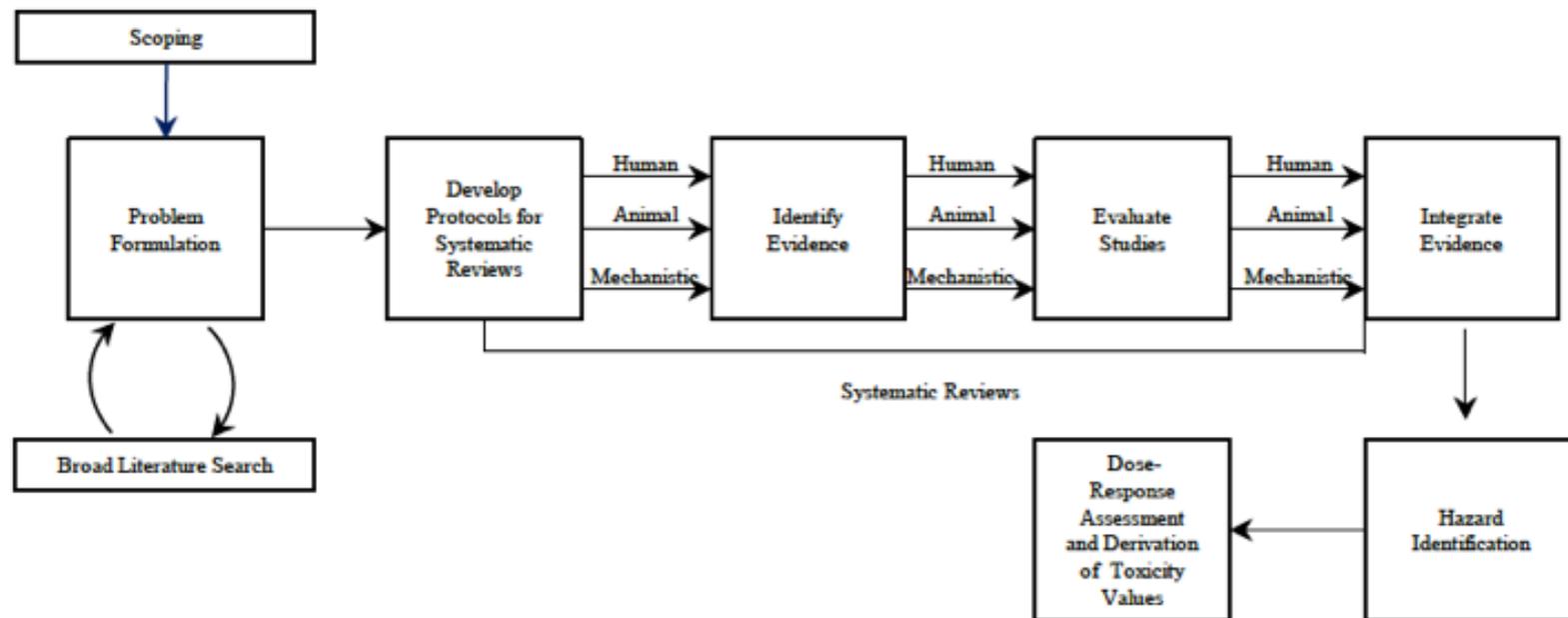
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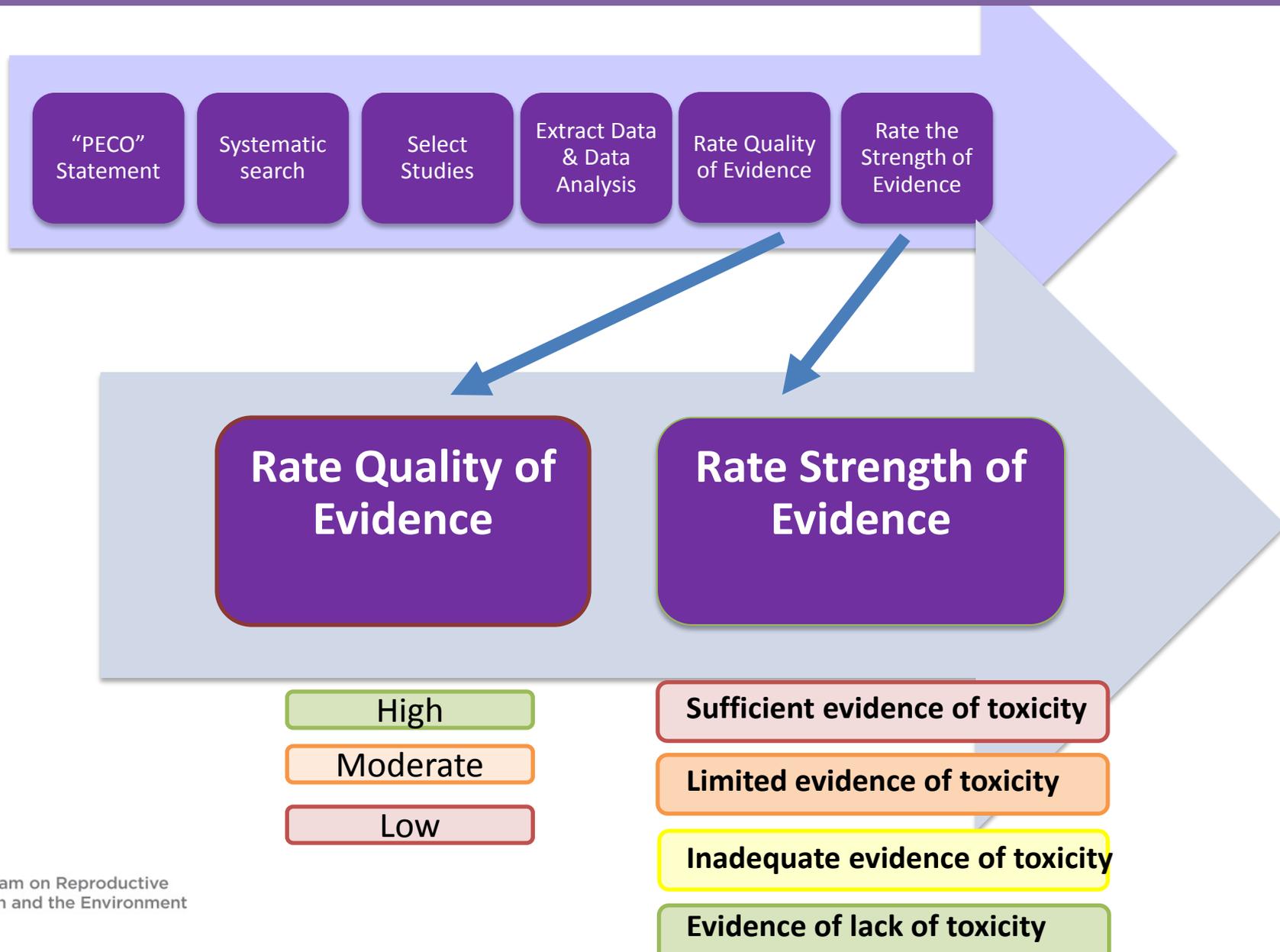
NTP

National Toxicology Program
U.S. Department of Health and Human Services

Evaluate each evidence stream separately using systematic and transparent approaches



Rate the Quality and Strength of the Evidence



Rate Quality of Evidence

- Risk of Bias



Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

- Rating quality of evidence

GRADE

Structured Process for Quality of Evidence for PFOA



		Evidence Stream	
		Human	Non-human mammalian
Downgrade	Starting rating	Moderate	High
	Risk of Bias	0	-1
	Indirectness	0	0
	Inconsistency	0	0
	Imprecision	0	0
Upgrade	Publication bias	0	0
	Large magnitude effect	0	N/A
	Dose response	0	N/A
	All possible confounding would confirm negative result	0	N/A
	Grade	0	-1
	Final rating	Moderate	Moderate

Strength of Evidence

Non-Human Mammalian Evidence = “Sufficient”

CRITERIA:

1. Quality of evidence: **Moderate**
2. What is the direction of effect? **Decrease in fetal growth with PFOA exposure**
3. What is the confidence in the effect? **A new study would be unlikely to change the certainty in the direction of the effect**
4. Are there other compelling attributes of the data that influence certainty?

Sufficient evidence of toxicity

Positive association is observed in multiple studies or a single appropriate study in a single species. Conclusion is unlikely to be strongly affected by the results of future studies.





Strength of Evidence

Human Evidence = “Sufficient”

CRITERIA:

1. Quality of evidence: **Moderate**
2. What is the direction of effect? **Decrease in fetal growth with PFOA exposure**
3. What is the confidence in the effect? **A new study would be unlikely to change the certainty in the direction of the effect**
4. Are there other compelling attributes of the data that influence certainty?

Sufficient evidence of toxicity

A positive relationship is observed between exposure and outcome, where chance, bias, and confounding can be ruled out with reasonable confidence. The available evidence includes results from one or more well-designed, well-conducted studies, and the conclusion is “unlikely to be strongly affected by the results of future studies.”



Summary

- UCSF using the Navigation Guide methodology has demonstrated structured, systematic and transparent methods of evidence integration are feasible and desirable
- USEPA has made important progress toward improved methods through the arsenic assessment
- To advance implementation of the NRC review, we recommend USEPA:
 - Use standard protocols
 - Develop and implement a more complete method for evaluating quality of human, non-human and mechanistic studies using prespecified criteria ;
 - Develop and implement a structured process for integrating evidence; and
 - Support infrastructure for the advancement of systematic reviews.



Thank you



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