

# Pathways to Implementation of the NRC Recommendations

Tracey J. Woodruff, PhD, MPH  
Professor and Director  
UCSF Program on Reproductive  
Health and the Environment



Program on Reproductive  
Health and the Environment

# 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**

*Juleen Lam,<sup>1</sup> Erica Koustas,<sup>1</sup> Patrice Sutton,<sup>2</sup> Paula I. Johnson,<sup>2</sup> Dylan S. Atchley,<sup>2</sup> Saunak Sen,<sup>3</sup>  
Karen A. Robinson,<sup>4,5,6</sup> Daniel A. Axelrad,<sup>7</sup> and Tracey J. Woodruff<sup>2</sup>*

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

*Paula I. Johnson,<sup>1</sup> Patrice Sutton,<sup>1</sup> Dylan S. Atchley,<sup>1</sup> Erica Koustas,<sup>2</sup> Juleen Lam,<sup>2</sup> Saunak Sen,<sup>3</sup>  
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**The Navigation Guide—Evidence-Based Medicine Meets Environmental Health:  
Systematic Review of Nonhuman Evidence for PFOA Effects on Fetal Growth**

*Erica Koustas,<sup>1</sup> Juleen Lam,<sup>1</sup> Patrice Sutton,<sup>2</sup> Paula I. Johnson,<sup>2</sup> Dylan S. Atchley,<sup>2</sup> Saunak Sen,<sup>3</sup>  
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**The Navigation Guide Systematic Review Methodology: A Rigorous  
and Transparent Method for Translating Environmental Health Science  
into Better Health Outcomes**

*Tracey J. Woodruff and Patrice Sutton*

**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*



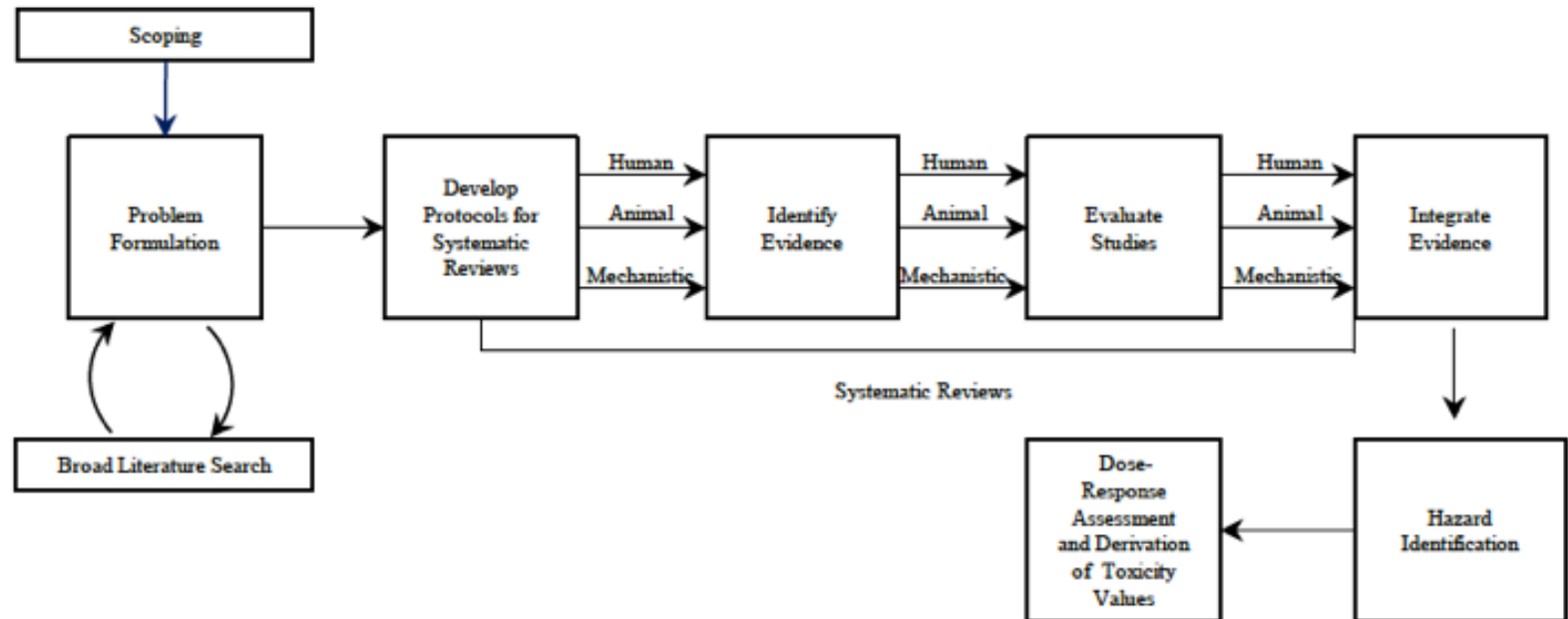
University of California  
San Francisco



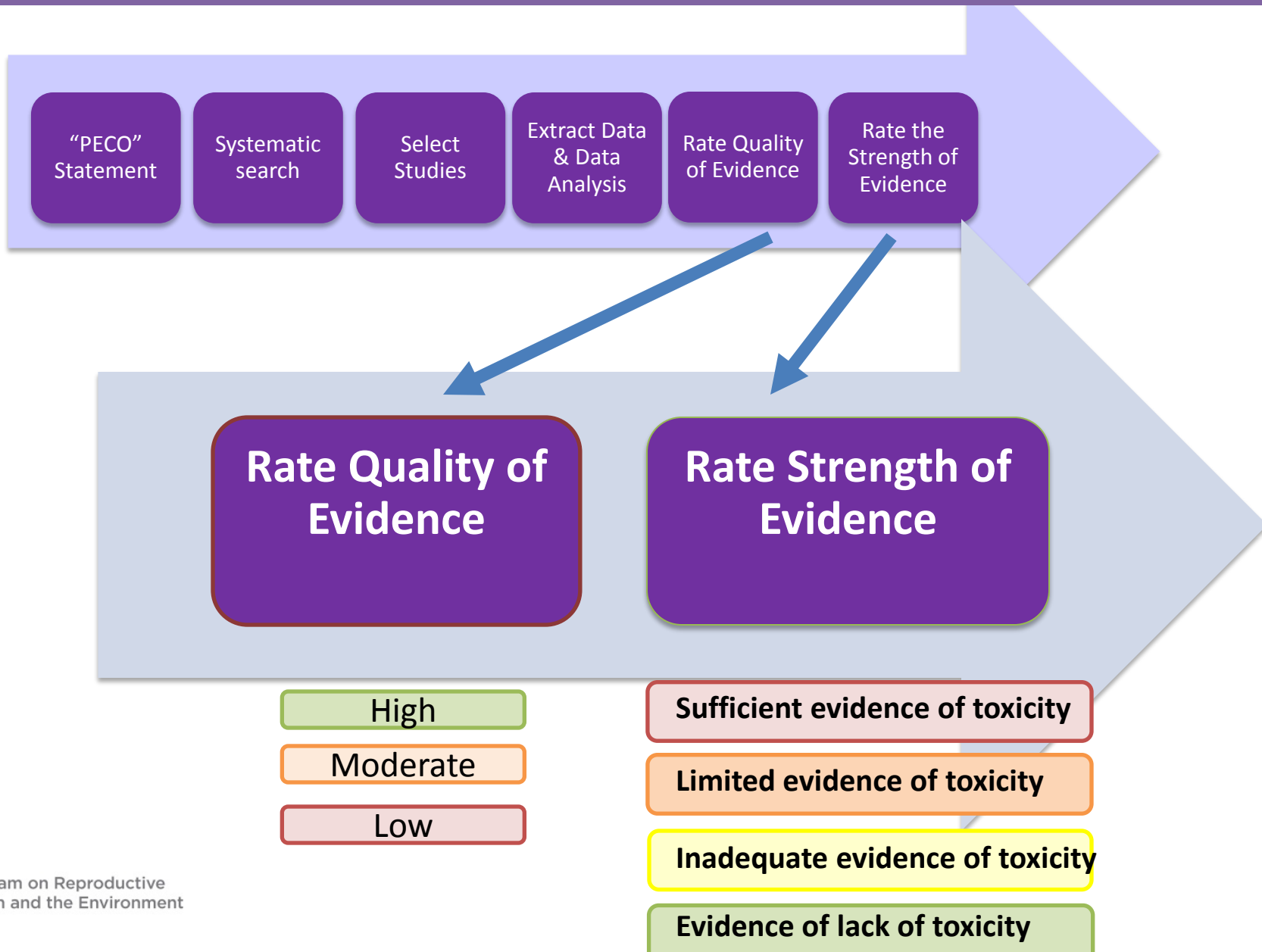
**NTP**

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
	<b>Final rating</b>	<b>Moderate</b>	<b>Moderate</b>

# 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



Program on Reproductive  
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University of California  
San Francisco

