Grouping and Toxicity Testing: Considerations for PFAS

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The American Chemistry Council (ACC)

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ACC is committed to improved environmental, health, safety and security performance through Responsible Care®; common sense advocacy addressing major public policy issues; and health and environmental research and product testing.

ACC members and chemistry companies are among the largest investors in research and development, and are advancing products, processes and technologies to address climate change, enhance air and water quality, and progress toward a more sustainable, circular economy.

PFAS Grouping: Refining Categories

- Grouping in the NTS based on structural and (limited) physicochemical properties

- ACC agrees PFAS should not be treated as a homogenous class of substances
  - An overly broad definition of PFAS is unscientific
  - It would also drain resources unnecessarily and hinder a focus on priority issues and exposures
  - We support a continued focus on risk incorporating consideration of both hazard and the potential for exposure

PFAS Grouping: Refining Categories

- ACC supports the approach taken in the testing strategy to prioritize groups or subgroups of PFAS. However we have concerns regarding:
  - The basis for the categories that have been identified
  - The lack of transparency on the categories that EPA has identified
  - An apparent loss of focus on priority issues and exposures
- ACC notes there are many more considerations than structure/limited phys. chem. properties that can inform grouping! (next slide)

PFAS Grouping: Refining Categories

- We suggest the concept of sub-class may be helpful:

"A 'Sub-class of Chemicals' means a group of chemicals within a broader class wherein analysis of

- structure,
- physico-chemical properties,
- composition,
- computational bioactivity profiles,
- toxicokinetics,
- mechanism/mode of action (similarity in eliciting molecular initiating events, key intermediate events, and other relevant computational and in vitro information and data)
- and available traditional toxicological and ecotoxicological testing data

indicates members of the sub-class are likely to all show the same type and approximate value, or show predictable trends as one moves up and down the sub-class,

for the specific toxicological or another property that is to be inferred."

PFAS Grouping: Refining Categories

- Advantages of a sub-class approach
  - Greatly expands grouping options
  - Provides a scientific basis for refining categories
  - Supports subsequent read-across for data gaps

PFAS Toxicity Testing:

Advancing Methods

- Toxicity testing in the NTS is tiered and reads-across to the other members of the category (aka ‘group’)
  - Testing via TSCA Section 4 test orders
    - Section 4 can be a useful tool for developing information on PFAS
    - There is already a significant amount of information for many of these substances and ACC supports the Agency’s efforts to collect that information prior to issuing a test order
    - Unclear how issued test orders are informing the rest of the category

PFAS Toxicity Testing:

Advancing Methods

- ACC generally supports both tiered testing (specified in TSCA Section 4) and read-across
  - Maximizing tiering would reduce testing costs and allow for more timely development of relevant information

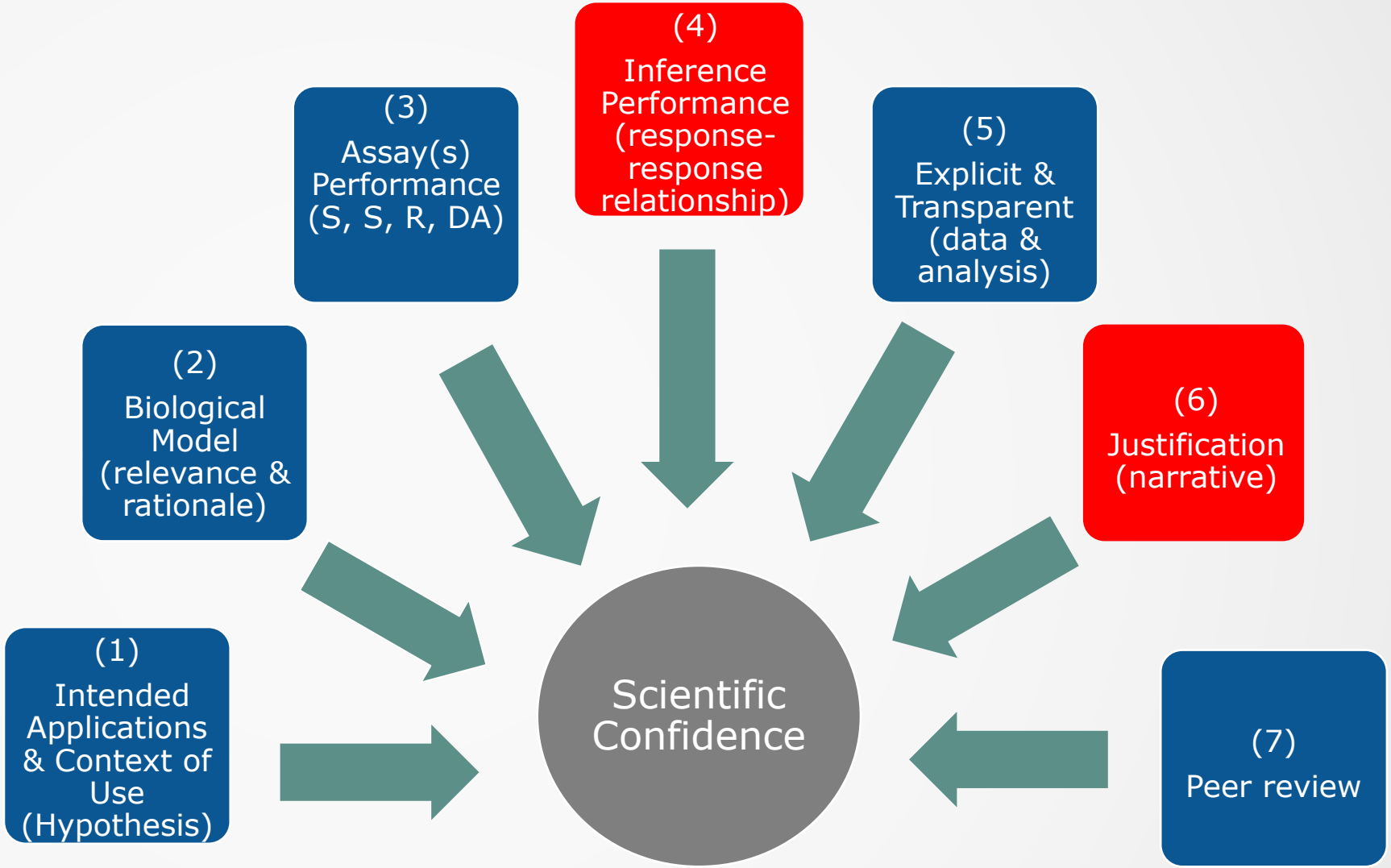
- Maximizing tiered testing
    - More NAMs could potentially be considered in existing tiers and/or additional tiers, if the requisite scientific confidence can be developed (next slide)
    - Missed opportunities to consider exposure (Dr. P. DeLeo, ACC presentation)

PFAS Toxicity Testing: Advancing Methods

- Scientific Confidence Frameworks (SCFs) to ensure NAMs have requisite scientific confidence
  - Provides an alternative to traditional ‘validation’
  - Can be applied to any NAM
  - Allows evaluation of whether or not the NAM is ‘fit-for-purpose’
  - At least (2) SCFs are currently available
    - van der Zalm et al. 2022[1]
    - ACC’s

[1]van der Zalm AJ, Barroso J, Browne P, Casey W, Gordon J, Henry TR, Kleinstreuer NC, Lowit AB, Perron M, Clippinger AJ. A framework for establishing scientific confidence in new approach methodologies. Arch Toxicol. 2022 Nov;96(11):2865-2879. doi: 10.1007/s00204-022-03365-4. Epub 2022 Aug 20. PMID: 35987941; PMCID: PMC9525335.

PFAS Toxicity Testing: Advancing Methods



Wrap-Up

- Adopting a sub-class approach may expand grouping and read-across options
- Maximizing tiered testing may help to accelerate the NTS
- Adopting an SCF may more rapidly advance confidence in NAMs for use both in the NTS and EPA-wide