WHO Initiatives to Evaluate PFAS (Phase 1)

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World Health Organization

Overview of Phase 1 (2024-2025)

- Developed novel methodology and used it to conduct landscape review to identify and prioritize key health effects and key ingested/occurrence of PFAS
- Developed preliminary general methodology to derive health-based guidance values (e.g., TDIs) for ingested PFAS (e.g., food and drinking water)
  - Protocol for systematic evidence collection and evaluation in Phase 2 considering best practices
  - Consideration of individual PFAS and PFAS mixtures
  - To be refined in Phase 2 based on prioritized ingested PFAS and health effect categories
- Set the stage for Phase 2 beginning Fall 2025

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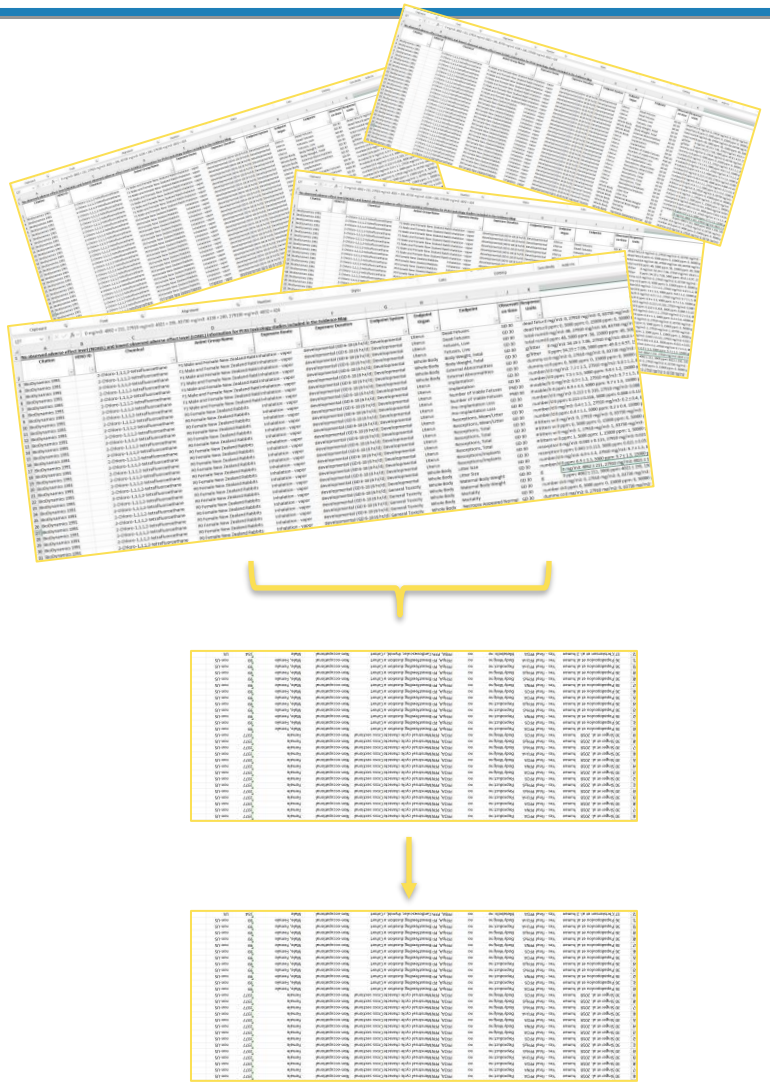
Objective of PFAS Landscape Review

To categorize and visualize existing literature to guide future research in Phase 2

- **HOW:** Compile databases from existing evidence maps, scoping and SRs into a composite database
- **WHY:** Use systematic and transparent methods, considering global information, without reinventing the wheel
  - **To identify *and prioritize* key ingested PFAS** (based on occurrence in food, water, and biomonitoring information)
  - **To identify *and prioritize* key health effects of PFAS** (as reported in existing evidence maps and databases)



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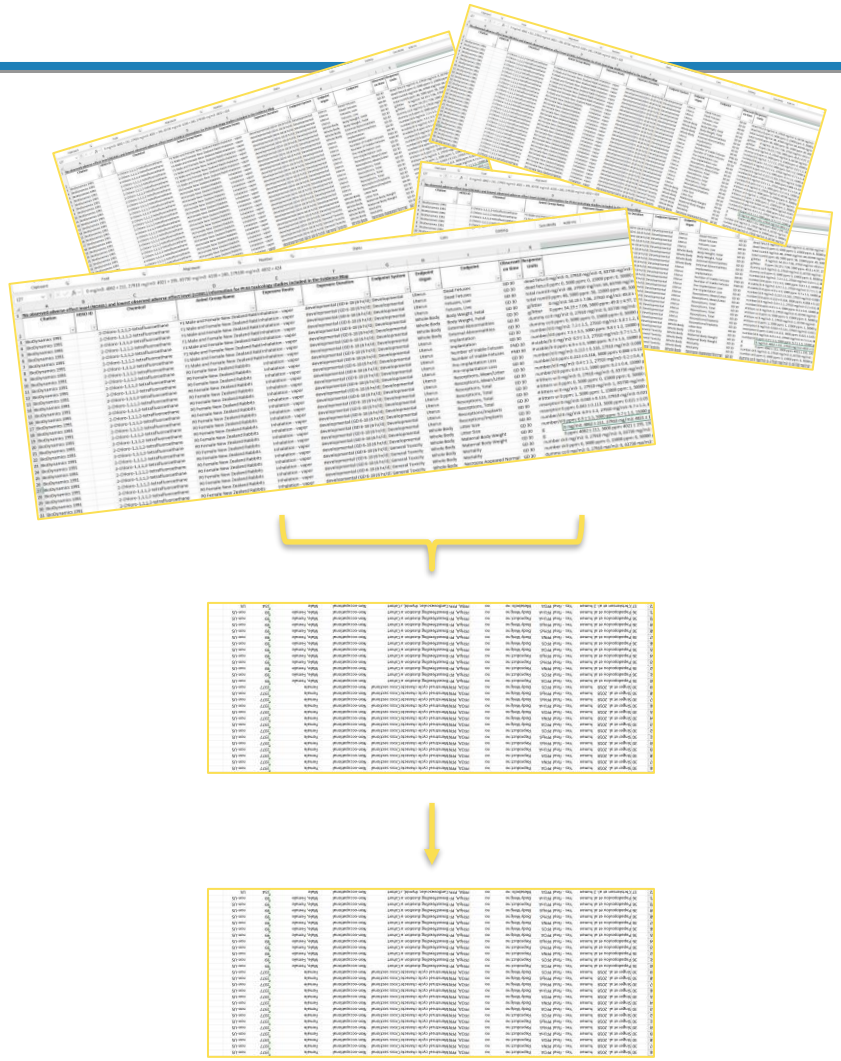
Data management challenges

- 1000+ columns of information/data
  - Authors' capture different information
  - Authors' capture same information differently
  - WHO Technical Advisory Group on PFAS helped decide what info/data to use for prioritisation
- Careful to avoid "apples-to-oranges" comparisons with merging databases
  - Loss of granularity to ensure decisions based on apples-to-apples comparisons



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Landscape Review of Occurrence

- Compiled 49 databases of systematic evidence maps and reviews
  - *General search: e.g., PubMed/ MEDLINE, Scopus, Web of Science, EMBASE*
  - *Occurrence databases/websites: country, regional, and international-level*
- Environmental occurrence
  - Limited data reporting by authors
- Human biomonitoring
  - *e.g., serum, plasma, urine, breast milk, hair*
- **~300,000 observations among 77 PFAS**

Landscape Review of Health Effects

Expanded Systematic Evidence Map for Hundreds of Per- and Polyfluoroalkyl Substances (PFAS) and Comprehensive PFAS Human Health Dashboard

Systematic Evidence Map for Over One Hundred and Fifty Per- and Polyfluoroalkyl Substances (PFAS)

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Systematic Evidence Mapping of Potential Exposure Pathways for Per- and Polyfluoroalkyl Substances Based on Measured Occurrence in Multiple Media

Epidemiology Evidence for Health Effects of 150 per- and Polyfluoroalkyl Substances: A Systematic Evidence Map

Per- and polyfluoroalkyl substances and human health outcomes: An umbrella review of systematic reviews with meta-analyses of observational studies

The PFAS-Tox Database: A systematic evidence map of health studies on 29 per- and polyfluoroalkyl substances

Non-targeted metabolomics and associations with per- and polyfluoroalkyl substances (PFAS) exposure in humans: A scoping review

A systematic evidence map of chronic inflammation and immunosuppression related to per- and polyfluoroalkyl substance (PFAS) exposure

- Identified and combined 48 databases of existing systematic evidence maps and reviews
- Differences in
  - PFAS
  - Data reporting
  - Terminology
  - Health endpoints
  - Other differences
- **~57,000 observations among 66 PFAS**

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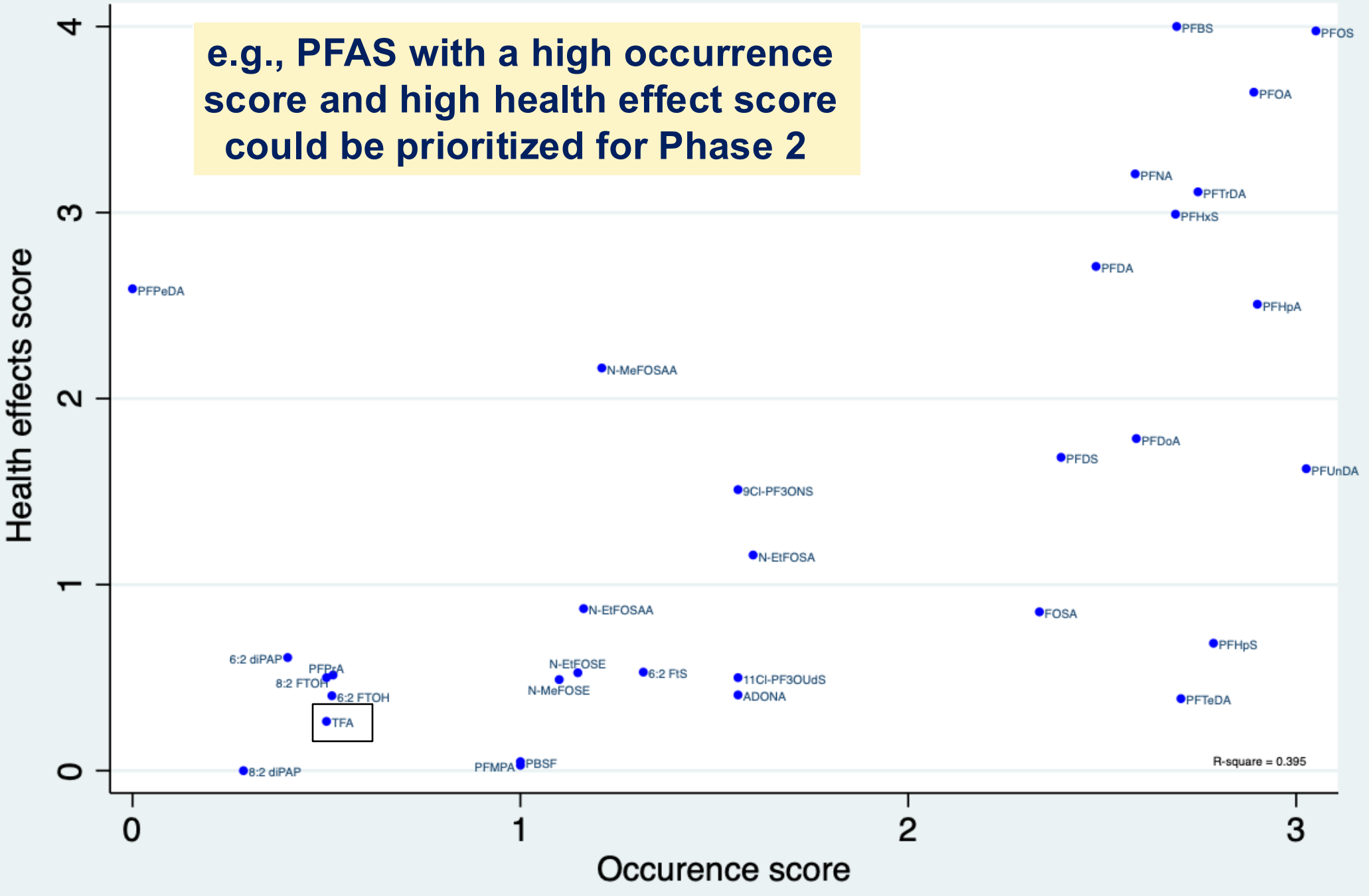
Results of Phase 1

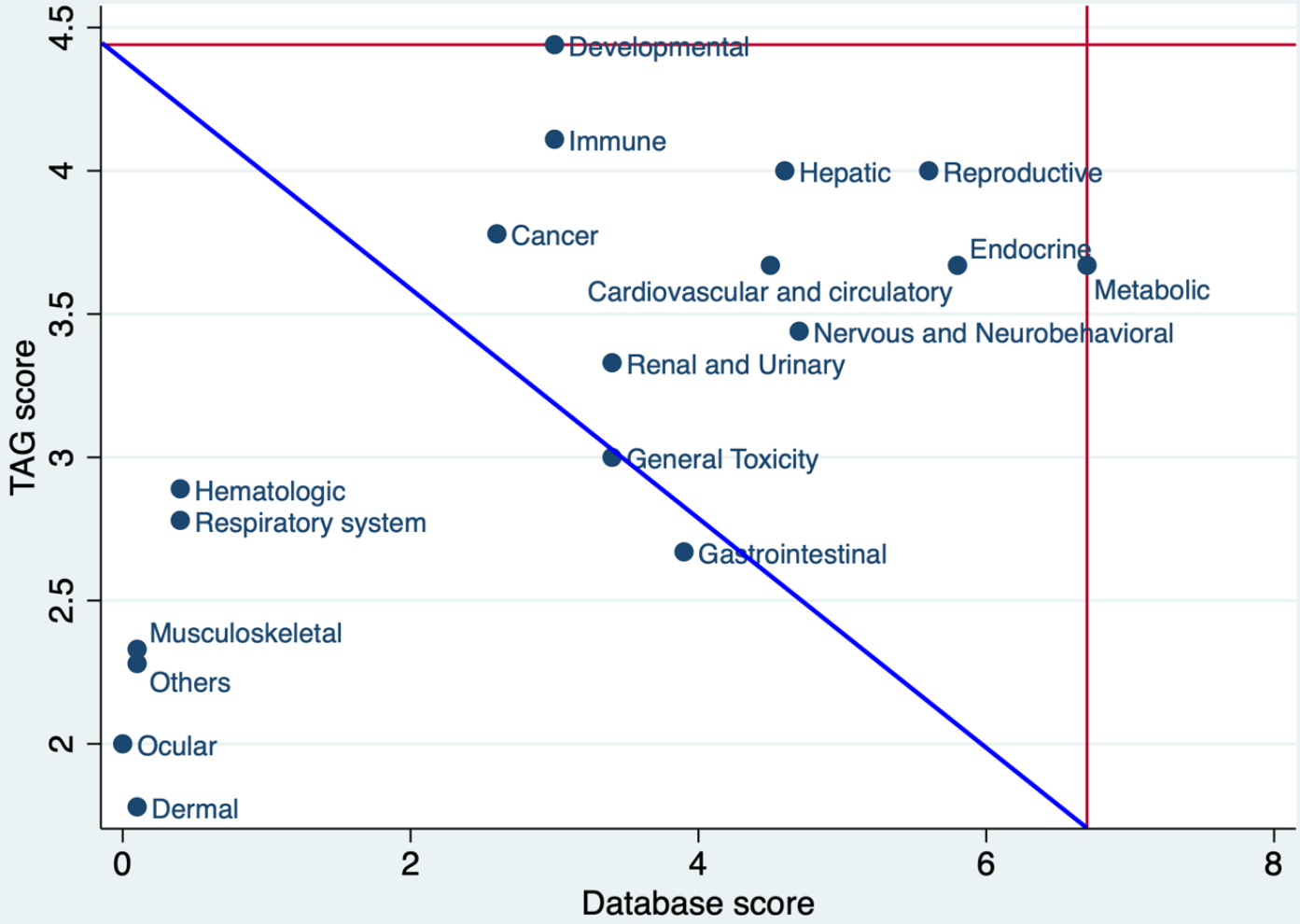
- Landscape review results
  - Compiled databases from systematic evidence maps and reviews of PFAS health effects and occurrence **identified 77 ingested PFAS and 18 health effects categories**
  - Based on algorithms developed by TAG-PFAS to weight the information most relevant to identifying key ingested PFAS and key health effects, **18 ingested PFAS and 6 health effects categories were prioritized for Phase 2**
- Proposed methodology to derive health-based guidance values for PFAS, including systematic evidence collection and evaluation and for consideration of individual PFAS and PFAS mixtures
  - To be further refined in Phase 2 based on the prioritized PFAS and health effects

32 PFAS intersect on occurrence and health effects landscape reviews

e.g., PFAS with a high occurrence score and high health effect score could be prioritized for Phase 2



Prioritization of 6 health effect categories



Phase 2:

Cancer
Developmental
Hepatic
Immune
Metabolic
Reproductive

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Protocol for **Systematic Evidence Collection and Evaluation** supporting health-based guidance value derivation for PFAS

Step 1. Define the key health effects and selected PFAS (WP1) and only perform search for 'PFAS + key health effect' combinations.

Step 2. Prioritize and subdivide systematic review tasks based on types of data to avoid doubling and to allow an overview of data.

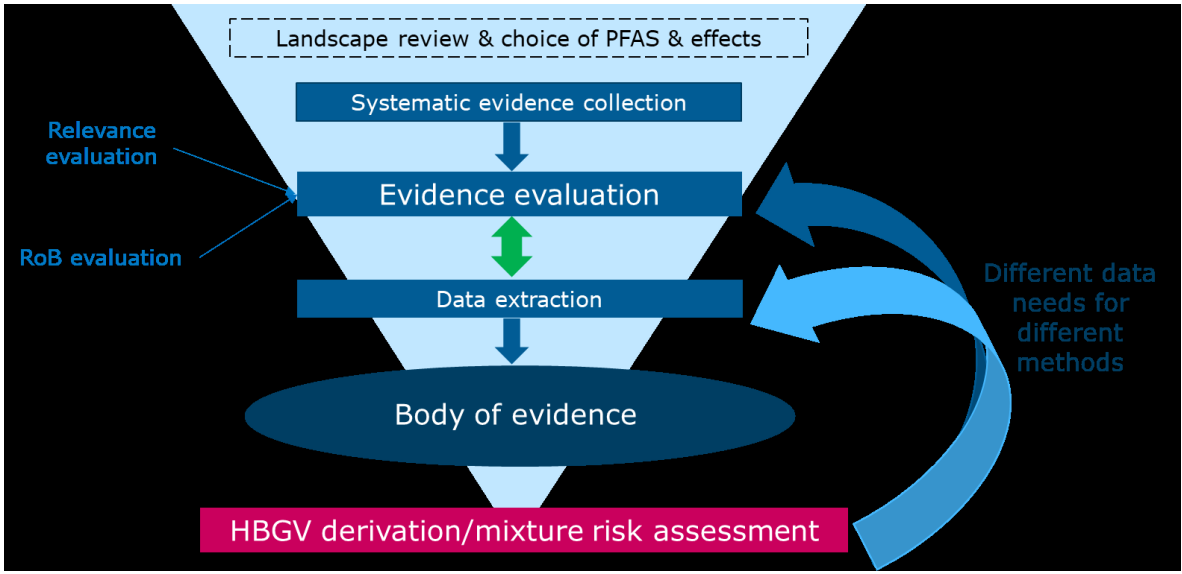
Step 3. Relevance sorting of data according to defined inclusion and exclusion criteria.

Step 4. Search which PFAS studies have evaluations available in HAWC (or other db) and compare to list of relevant studies.

Studies already evaluated for RoB do not need a new evaluation. Study data already in a database does not have to be re-extracted.

As an example, if an RPF approach is chosen: Define an index compound (IC) and perform full systematic search, evaluation and data extraction for HBGV IC. A more confined (scoping) search, evaluation and data extraction can then be performed for PFAS RPFs and data to support grouping and human relevance. The latter may be iterative based on the data available.

Optional Step 5. Define a method based on the totality of the data and evaluate only study-types relevant to that method.



AVAILABLE ONLINE:

https://www.rivm.nl/publicaties/protocol-for-systematic-evidence-collection-and-evaluation-supporting-health-based#:~:text=This%20document%20outlines%20both%20the%20process%20and%20the,and%20evaluation%20%28SECE%29%20to%20support%20HBGV-derivation%20for%20PFAS.

Flowcharts and decision trees to group PFAS and for mixtures risk assessment

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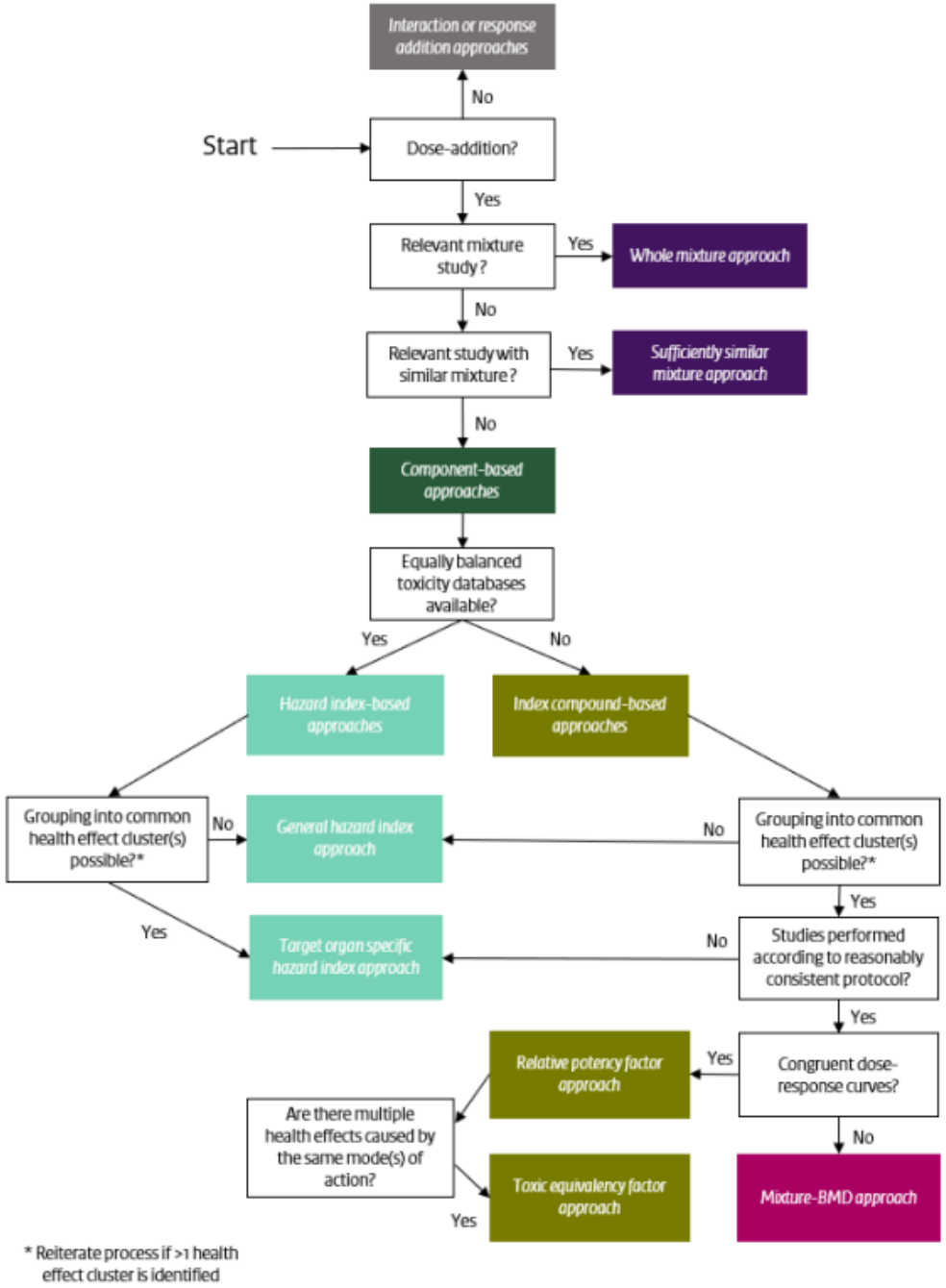
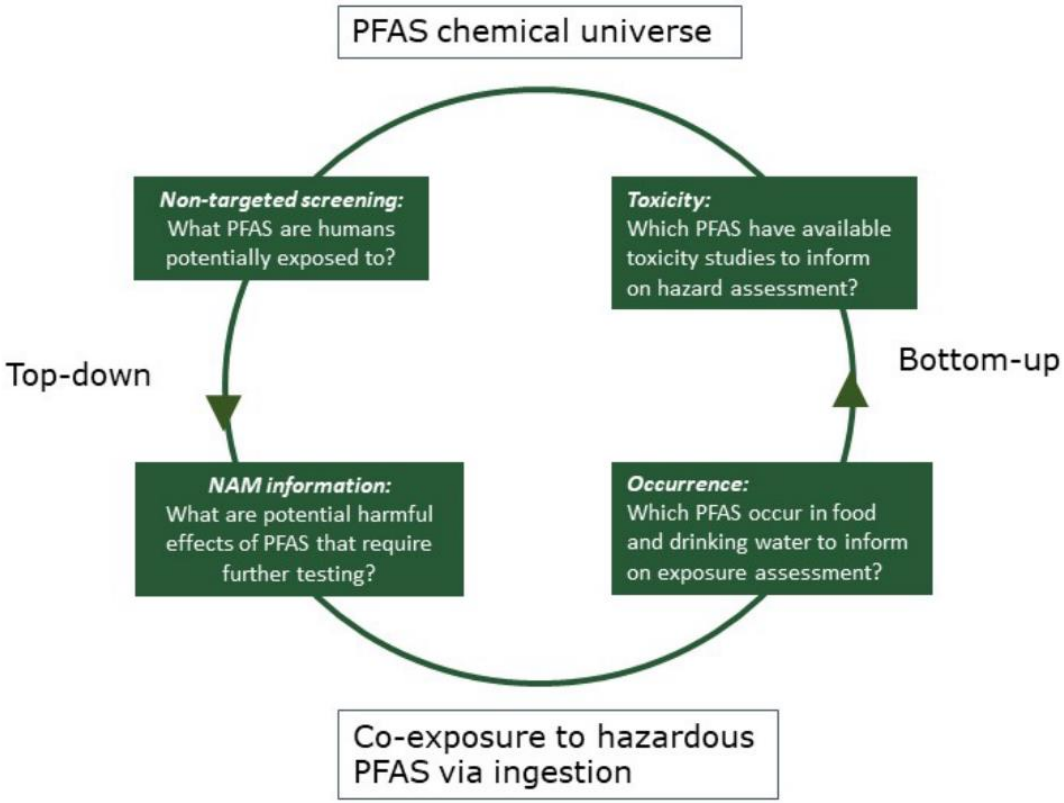


Mixture risk assessment approaches to evaluate oral exposure to PFAS



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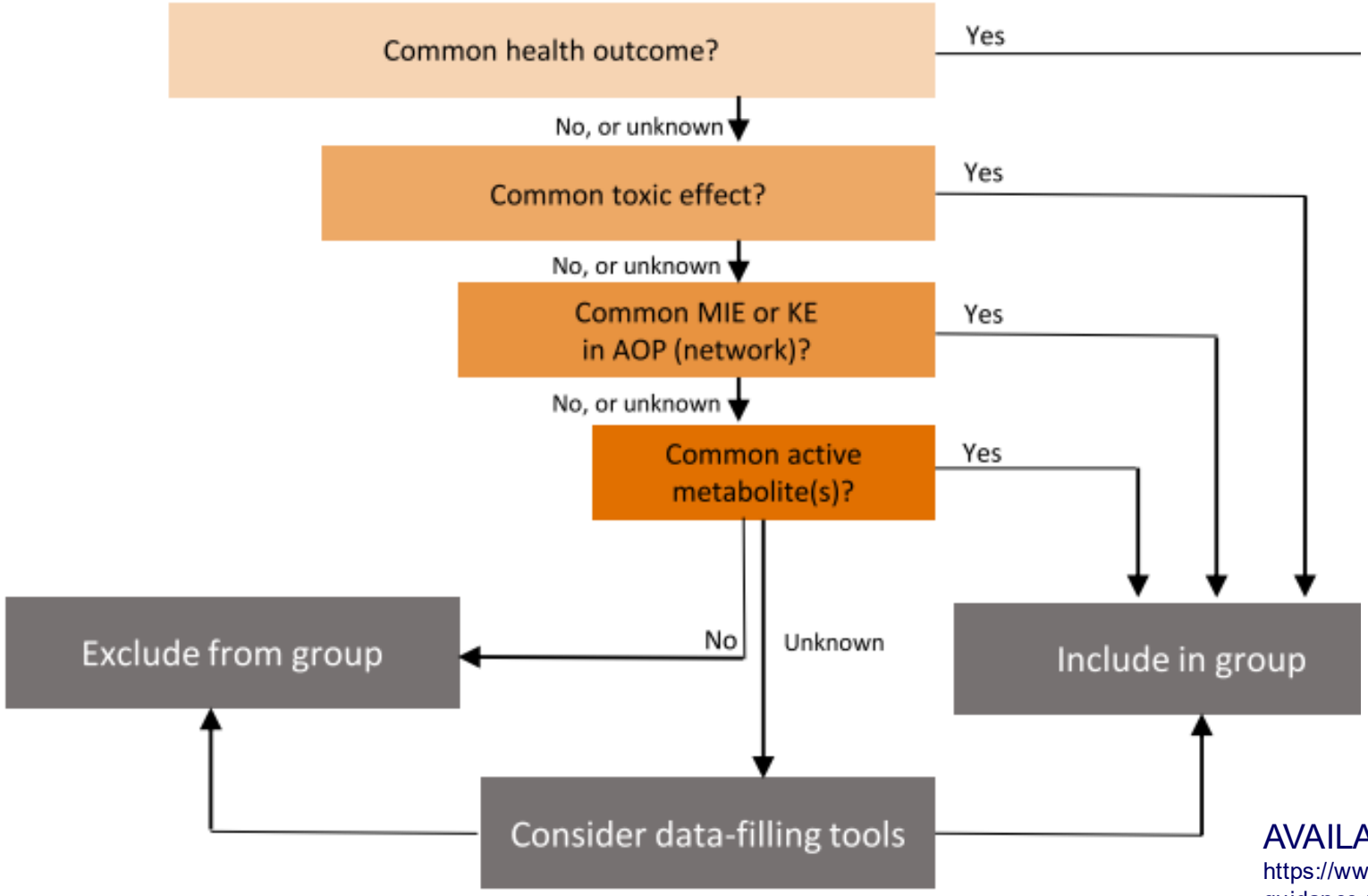
Flowchart cluster PFAS into health effect categories based on toxicological similarity (adapted from Rider et al., 2018).

Methodology for health-based guidance value (HBGV) derivation for PFAS (individually and in mixtures)



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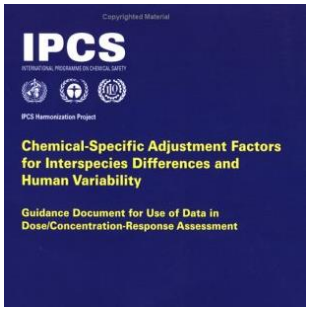
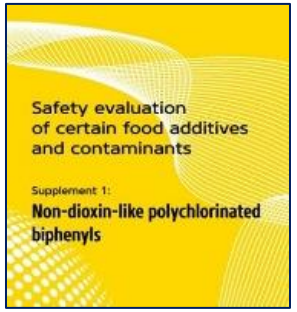
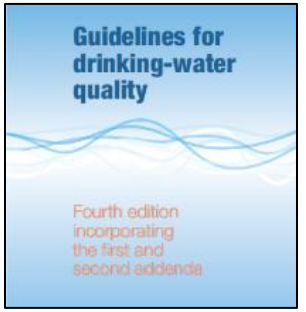
https://www.rivm.nl/publicaties/methodology-for-health-based-guidance-value-hbgv-derivation-for-pfas-individually-and

WHO Initiatives to Evaluate PFAS

- Phase 2 (2025-2027, supported by EC and others)
  - Convene 2nd Technical Advisory Group on PFAS Assessment
  - Key activities
    - *Systematic evidence collection and evaluation of 6 health effect categories for up to 18 PFAS prioritized from Phase 1*
    - *Select groupings for mixtures risk assessment and identify risk assessment approach(es) for individual PFAS and/or PFAS mixtures*
    - *Propose a range of health-based guidance values*
- Set the stage for WHO-FAO Joint Expert Meeting on Food Additives (JECFA) and Guidelines for Drinking-water Quality (GDWQ) expert group assessments of PFAS begins 2027







Final WHO guideline values for drinking-water will consider pragmatic aspects

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