# Application of Toxicity-Based Read Across Methods for PFAS Hazard Identification in Risk Assessments

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**Background/Objectives.** Several per- and polyfluoroalkyl substances (PFAS) have been detected in environmental media across the United States at hazardous waste sites. There is limited PFAS toxicity information and regulatory thresholds for use during hazard identification and human health risk assessments when characterizing a site and making risk-management decisions about remediation. However, the advancements in New Approach Methods (NAMs) have led to read-across tools to predict the potential toxicity of PFAS with limited data. USEPA has developed a beta-version of a generalized read-across (GenRA) tool that is publicly available (https://comptox.epa.gov/dashboard). The objective of this study was to evaluate the potential application of USEPA's beta-GenRA tool during hazard identification in a site investigation or risk assessment. GenRA was used to predict and evaluate toxicity-based points of departure (PODs) and potential screening reference doses (RfDs) for select PFAS that have limited toxicity data and compare these with values from the literature or regulatory agencies.

**Approach/Activities.** PFAS commonly detected in environmental media at hazardous waste sites in the United States were selected for this read-across application. The following steps were used to estimate PODs and estimate potential screening RfDs for each target PFAS:

- Toxicity analogues for the target PFAS were identified using USEPA's GenRA tool in the CompTox dashboard through chemical fingerprints (e.g., Morgan fingerprint/Tox Print/ToxCast/Custom).
- At least two analogues were selected per target PFAS based on the nearest similarity index.
- GenRA prediction and read-across was run to obtain potency doses from animal studies for each analogue.
- Information available from the literature regarding toxicity trends between the target PFAS and analogue was considered and incorporated.
- The similarity weighted activity read-across method was employed to estimate a POD for the target PFAS from potency doses for analogues.
- Standard USEPA uncertainty factors were applied to estimate potential screening RfDs for the target PFAS.

**Results/Lessons Learned.** The estimated PODs and potential screening toxicity RfDs for the target PFAS were compared to the PODs, RfDs, and toxicity information available in the literature and from regulatory agencies. The limitations, challenges, professional judgment needed, and uncertainties associated with estimating PODs and calculating potential screening RfDs derived using the read-across method were identified. A strategy for applying read-across methods to identify potential hazards/risks will be discussed, which can be used during PFAS preliminary assessments, supplemental investigations, or remedial investigations. Read-across NAMs are used in the USEPA Toxic Substances Control Act (TSCA) and pesticide programs and are part of USEPA's 2019 PFAS Action Plan (www.epa.gov/pfas/epas-pfas-action-plan) to reduce uncertainties arising from limited PFAS with consensus toxicity data.