

## **Evaluation of USEPA's Generalized Read-Across (GenRA) and Selected Example Case Studies to Identify Challenges and Recommendations to Consider for GenRA Improvements**

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Read-across is a technique for information gap filling to estimate a property (e.g., a hazard effect dose level) of a substance using inference based on empirical data of similar substances. GenRA has been designed by EPA to transition read-across from what has typically been an expert judgment-based approach to a more systematic, transparent and data-driven approach. In its current form, GenRA is focused solely on structural or bioactivity predictions. At this time, other contexts of similarity, such as metabolism and toxicokinetics, are not considered. While the information available from USEPA on GenRA describes all of the components of this read-across approach, ACC's LRI Strategic Science Team (LRI-SST) has not yet critically evaluated the underlying methods. As it is anticipated EPA's programs, particularly TSCA, will increasingly turn to read-across and use GenRA to fill toxicity information needs, understanding the strengths, limitations of the components of GenRA and confidence in inference of toxicity values generated by GenRA is critical. Based on such an analysis, specific research and development activities to improve the performance of, and confidence in, read-across can be developed and considered.

### **Implications:**

A thorough review of EPA's generalized read-across (GenRA) approach will be conducted to include evaluation of computational tools for identification of chemical analogs/similarities, as well as understanding the decision points applied to activity/bioactivity data. This evaluation will inform on the strengths and limitations of GenRA and will facilitate interpretation of the output. This information will be used to further guide discussions on potential future research efforts to improve GenRA and build confidence in its use by stakeholders.

**Key words:** GenRA, generalized read-across, toxicity, analysis

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