Data Gap Assessment and Predictive Toxicology

Overview – Assessment of toxicology for a chemical substance without data has traditionally been accomplished primarily through the use of a nearest analog, read-across approach. In many cases, data for analogs may be lacking and the resulting assessment may have data gaps. Addressing these data gaps can be important for a variety of reasons: developing SDS sheets or other hazard statements, reducing the monetary and animal costs of testing, and supporting regulatory filings.

Recent updates to the Toxic Substance Control Act (TSCA21) have resulted in an increased need to address data gaps. With this updated law, the EPA has new latitude for requiring testing for new chemical submissions and the ability to reject or regulate New Chemical Substance notifications based on data gaps. To maximize submission success, it is important to predict the toxicological hazard your chemical may present for all possible endpoints. Often, this can be done with alternative methods to animal testing, such as predictive models or in vitro testing. While there are no drop-in *in vitro* replacements for any given *in vivo* endpoint, there are increasingly sophisticated computational methods and testing strategies that can help fill data-gaps without animal testing.

CERM's lead toxicologist, Dr. Alexandra Maertens, is the head of the Read Across/Big Data initiative at Johns Hopkins Bloomberg School of Public Health, and has extensive experience with computational toxicology. CERM has completed hundreds of chemical hazard assessments, using a variety of predictive methods. We are at the forefront of this emerging area of science and can help find and address toxicological data gaps. Options can include *in vitro* assays, QSARS, or PBPK models – all of which can help clarify hazards quickly, with less expense and hassle than an agency-mandated animal test. For some endpoints (i.e. skin sensitization, skin corrosion, and eye irritancy) often a combination of *in vitro* assays will be accepted by regulatory agencies. For other, more complex endpoints, it is possible to formulate an assessment that will be accepted by the regulatory agencies depending on the available analog data. Additionally, something as simple as a dermal absorption model can go a long way towards convincing regulatory agencies that hazard can be appropriately controlled.

Data Gap Assessment – CERM can complete a hazard and data gap assessment for a chemical substance, either in support of a PMN filing, other regulatory filings, a Pollution Prevention (P2) framework screening level assessment, or other instances where a toxicological profile may be needed. The assessment consists of three steps: assessing data gaps, assessing data availability, and developing an appropriate strategy to address specific data gaps.

The traditional way to address a data gap is to do a read-across or weight-of-evidence approach; however, in many cases, lack of appropriate analogs or supporting evidence may lead to remaining gaps. If further clarification is needed, often a QSAR can provide adequate evidence even if the data is too sparse for a direct read-across approach. In other cases, PBPK models can be useful in demonstrating that a likely internal dose is minimal. If the model or available data is inadequate, it may be possible to identity *in vitro* tests that can rule out potential hazard relatively quickly and more cost-effectively than traditional animal testing.

In many cases, CERM can find ways to adequately address these gaps without the need for time consuming and costly animal testing.

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