

Begin with the End In Mind: A First Step in the Path Towards Data Enabled Predictive Modeling for Nano-EHS

Justin Teeguarden, PhD, DABT

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Purpose

Assemble ideas and opinions regarding how best to organize, enable and initiate research and infrastructure to support data-enabled predictive modeling in nano-EHS related activities.



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Why do we Need Prediction in Nano-EHS?

- ▶ Toxicologically new class of materials
- ▶ Vast number of potential materials
- ▶ Rapid development, rapid introduction into commerce
- ▶ Toxicology testing, exposure studies, environmental studies limited by both time and resources.
- ▶ Organizing ourselves around a paradigm of prediction is simple the most responsible way to address EHS issues
 - Makes the most use of data and resources

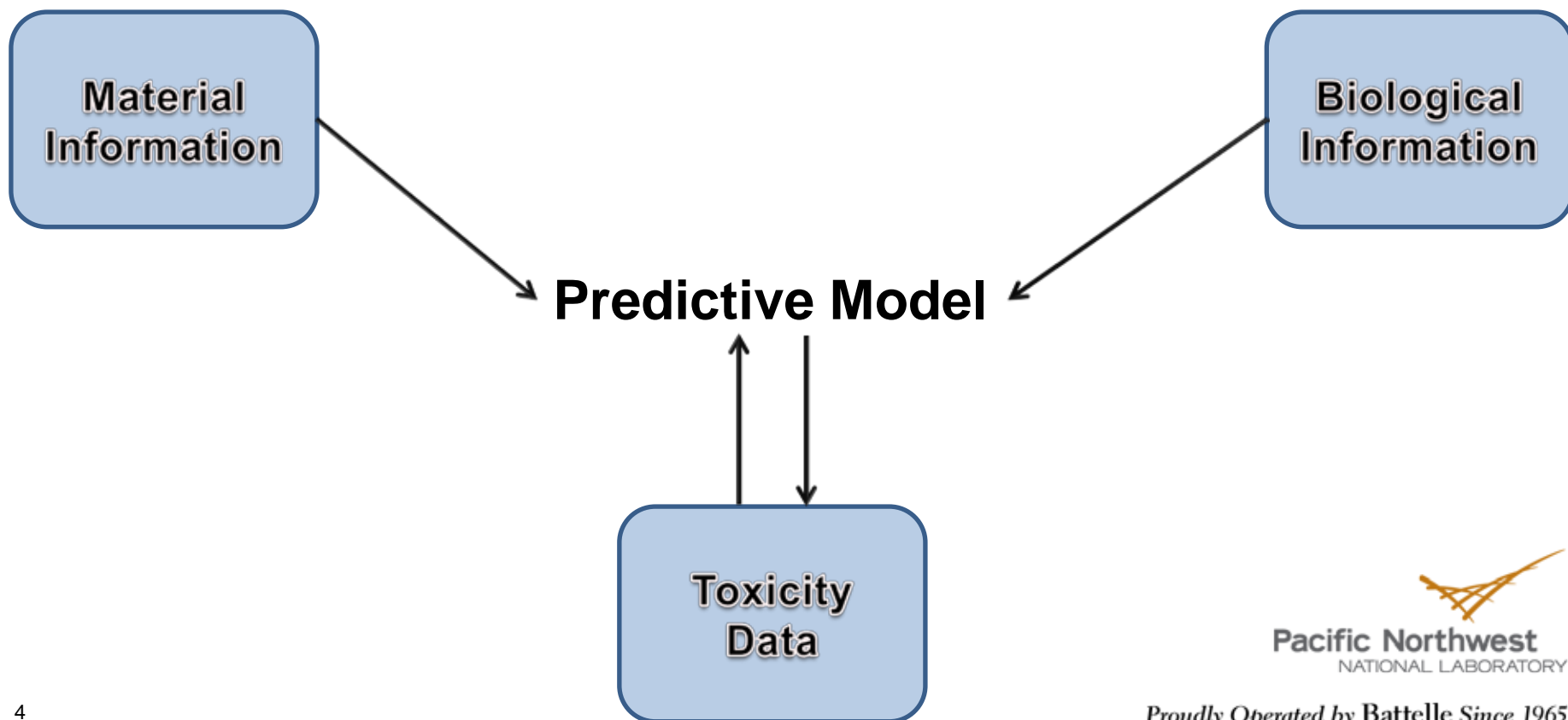


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What is Predictive Modeling in Toxicology?

The application of quantitative, relational or statistical models to predict hazard, toxicity or dose from biological, toxicological, and chemical/material information



How Has Predictive Modeling Been Used?

- ▶ Classification
 - Discrimination between genotoxic and non-genotoxic carcinogens.
 - Genomic signatures of carcinogens and non-carcinogens
 - Bio-signature of 37 genes, >80% accuracy for identifying carcinogens from non-carcinogens
- ▶ Structural features related to genotoxicity, pharmacologic activity, and toxicity.
- ▶ Size dependent deposition of particles in the upper and lower respiratory tract



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How has Predictive Modeling Been Used?

- ▶ Prediction and extrapolation of pharmacokinetics & dosimetry across route, dose and species.
- ▶ Environmental fate and transport



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What Needs Prediction in Nano-EHS?

- ▶ Exposure, temporal and spatial variation, agglomeration
- ▶ Environmental fate
- ▶ Dose—in vitro, in vivo, high dose-low dose, cross species
- ▶ Classification
 - Ranking for further testing
 - Exposure
 - Hazard potential
 - Potency
 - Mode of action



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Prediction Requires an Understanding of the System, Quantitative Tools and Data



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