

Leveraging the New Predictive Toxicology Paradigm in Evaluating Emerging Technology

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There are significant gaps in information concerning the environmental health and safety impacts of chemicals. The high cost and uncertainty associated with conventional testing approaches is exacerbated in the context of rapidly emerging materials and products such as nanomaterials. The role that a new predictive paradigm could play in regulatory decision-making is uncertain especially in regards to emerging technologies, such as nanomaterials. The objective of this project is to reduce this uncertainty by examining the ways in which emerging predictive toxicology methodologies could be used by the EPA in section 4 final test rule promulgation.

A new paradigm of predictive toxicology presents a possible solution for agencies to handle the speed in which new substances and materials are being developed. This new paradigm uses data regarding perturbations of cellular responses and of physicochemical properties of materials generated by *in vitro* tests and computational methods to predict toxicity. Such approaches have the potential to predict toxicity of more materials at a faster rate through rapid assessment approaches, such as high throughput screening, and computational approaches, such as advanced quantitative structure activity relationships (QSARs). Advances in toxicity testing could achieve a paradigm shift away from conventional *in vivo* approaches toward increased use of *in vitro*, *in silico*, or tiered testing approaches.

Section 4 of the Toxic Substances Control Act (TSCA), 15 U.S.C. §2601 et seq. (1976), authorizes the EPA to require testing of a chemical substance or mixture to address insufficient information on the environmental health and safety effects of the material. Where the EPA makes certain findings such as determining that a chemical “may present an unreasonable risk of injury to health or the environment,” the EPA may promulgate a rule requiring the manufacturer or processor to conduct specified tests or studies. The agency faces a substantial hurdle in promulgation of the test rule; its findings in support of the rule must be based on substantial evidence.

The paper will examine the potential opportunities for and constraints on the use of the new predictive paradigm in the case of Section 4. It will focus on two potential uses of predictive toxicology; namely (1) in establishing that testing is (or is not) required and (2) as part of the testing required in the Section 4 test rule. The paper will assess current EPA practices under Section 4 and the standards used by the courts in evaluating the need for testing as well as its scope and nature. It will evaluate the impact of those agency practices and judicial standards on the use of predictive toxicology, using carbon nanotubes as a case study.