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My Comment:

CLASSIFICATION: UNCLASSIFIED

Toxicologists understand that chemical-induced toxicity is dependent on dose rate. (Dose rate is used here to mean the dose, or external exposure, in units of weight of a chemical substance per unit of body weight per unit of time.) The chemical absorption, distribution, metabolism, and elimination pathways that maintain homeostasis involve time-dependent molecular interactions. Toxicity results when rate-limited homeostatic pathways are overcome and adverse outcome pathways switch in. In this regard, the NTP's strategy lacks essential precision in the measurement of time. The NTP's approach measures dose-rate in terms of mg/kg/day. To be relevant to the elucidation of molecular pathway dynamics, time measurement must be much more precise than 24-hours. It is essential that time be measured in at least units of seconds to be relevant. I suggest that application of real-time imaging and chemical sensor technologies presents an opportunity to overcome the limitations traditional dose-response strategies as well as the NTP proposed strategy for modeling dose-response from genomics data.

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