BY HOW MUCH DO SHAPES OF TOXICOLOGICAL DOSE-RESPONSE RELATIONSHIPS VARY?

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A re-analysis of a large number of historical dose-response data for continuous endpoints showed that the shapes of the dose-response relationships were surprisingly homogenous. The datasets were selected on the sole criterion that they were expected to provide relatively good information on the dose-response shape, and included a variety of endpoints and both in vivo and *in vitro* studies of various types. Both the four-parameter exponential and Hill model adequately described all toxicological dose-response data we considered. For a given endpoint and study type, dose-response shapes did not differ statistically significantly among chemicals in the *in vitro* studies considered, while a mild among-chemical variation in the steepness parameter seemed to be present in the *in vivo* studies. These findings have various practical consequences. For continuous endpoints, model selection in the BMD approach is not a crucial issue. The often-applied approach of using constraints on the model parameters to prevent "infinite" slope at dose zero in fitting a model is not in line with our findings, and appears to be unjustified. Instead, more realistic ranges of parameter values could be derived from re-analyses of large numbers of historical dose-response datasets in the same endpoint and study type, which would then be used as parameter constraints or informative priors in the analysis of future individual datasets. This approach would be particularly useful for weak datasets (e.g. few doses, much scatter). In addition, this approach may open the way to use fewer animals in future studies. Finally, we argue that distinctions between linear, sub/supralinear or thresholded dose-response shapes, based on visual inspection of plots, are not biologically meaningful nor useful for risk assessment. *This abstract does not necessarily reflect EPA policy.*