Supplemental Guidance for Final Category Analysis

This supplemental guidance for final category analysis is developed by US EPA based on recommendations from the High Production Volume (HPV) Workgroup of the National Pollution Prevention Advisory Committee (NPPTAC).

This additional guidance will be an addendum to the US EPA's document "Development of Chemical Categories in the HPV Challenge Program" Section III, Step 8 A. Once all data, including those newly developed, justify the category, the sponsors need to perform final category analysis according to this guidance which then will be reviewed by US EPA. Please note that further changes in this guidance will be necessary as more experience is gathered. We strongly urge that the sponsors consider these recommendations for submitting their final category analysis to US EPA.[1]

Details of Category Analysis

The following are basic elements of the final category analysis:

Definition of the Category
Documentation for Data Derivation
Data Matrix

(1) Definition of the category

A statement of the definition and justification for the category that reflects all available data, including any new test data or estimated values developed through execution of the test plan. Any change in the category definition or justification from that provided in the original test plan, and how any chemicals removed from or added to the category to be assessed, should be explained.

(2) Documentation for Data Derivation

A thorough explanation should be provided for the method(s) of data derivation (i.e., extrapolation/interpolation) and rationale used by the sponsor to provide a "value" for each relevant endpoint for each untested category member.

(3) Data Matrix

A completed data matrix that provides the full data set for all category members for all relevant endpoints. This matrix should include assignment of an appropriate value to each cell of the matrix. Each value in the final data matrix should be accompanied by an indication of how it was derived (i.e., measured data, estimate derived from applying a SAR/QSAR, read-across, etc.).

(a) For category members not tested directly, the format/form (including units as applicable) in which the interpolated/extrapolated/estimated values for a given endpoint are expressed should match the format/form of the measured values for that same endpoint for the tested category

[1]US EPA recognizes that a great deal of work has been done by the Organization for Economic Cooperation and Development (OECD) with regard to category analysis, and the OECD is in the final steps of finalizing its category analysis guidance. [Organization for Economic Cooperation and Development. 2004. Revision of the Guidance Document for the Formation and Use of Chemical Categories has been published in Chapter 3, Section 3.2 in the *OECD Manual for the Investigation of HPV Chemicals*.]

members. The appropriate format/form will vary with endpoint and method of interpolation/extrapolation/estimation, but may include a single quantitative value, a maximum value (e.g., <X), a minimum value (e.g., >Y), a range (e.g., between X and Y), or, where appropriate, a qualitative descriptor (e.g., readily biodegradable, positive/negative). If a quantitative value or range can be provided, it should be, barring a compelling justification as to why it should not be.

(b) The interpolated/extrapolated values provided should be "stand-alone," and should not require accessing analogous data for other category members in order to be understood or interpreted. For example, use of a term such as "similarly toxic" should be avoided; rather, the quantitative value or range of values for the tested category member(s) serving as the basis for the interpolated/extrapolated value should be what is inserted into the matrix cell for the untested category member.

(c) Complex mixture and/or Class 2 substance (i.e., substances of unknown or variable composition) categories may warrant case-by-case consultation between the sponsor and OPPT in order to derive an acceptable category data matrix.

Surrogate Chemicals

An issue closely related to the use of categories is the use of so-called "surrogate chemicals" – chemicals not formally included in a category but judged to be sufficiently similar to an individual chemical or a category so that test data on one or more endpoints can be used to interpolate/extrapolate values to the sponsored chemical/category members. In such cases, the same elements described above for the category analysis document should be provided for the use of surrogates (unless already provided in the original test plan): an explicit justification for the selection and use of the surrogate for the relevant endpoints; a description of how values for the sponsored chemical(s) have been interpolated/extrapolated from the surrogate(s); and a data set that includes the actual interpolated/extrapolated values and indicates their source. [Note: The term "surrogate chemical" as used here is synonymous with the terms "supporting chemical" and "analogue."]

Completion of Category Analysis

The completed category analysis based on the supplemental guidance outlined above will be submitted to EPA. Upon EPA's review, the sponsors will be notified whether the category analysis is satisfactory or whether further work or clarification is needed.