

AN ALTERNATIVE METHOD FOR ESTABLISHING TEF<sub>s</sub> FOR DIOXIN-LIKE COMPOUNDS. PART 1. EVALUATION OF DECISION ANALYSIS METHODS FOR USE IN WEIGHTING RELATIVE POTENCY DATA

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**Introduction**

A number of investigators have recently examined the utility of applying probabilistic techniques in the derivation of toxic equivalency factors (TEFs) for polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) [hereafter referred to as "dioxin-like compounds"].<sup>1,2</sup> The current mammalian TEFs established by the World Health Organization (WHO)<sup>3</sup> represent single assigned point values despite the fact that they are derived from underlying distributions of individual REP values. It is believed that the use of a distributional approach will allow for better characterization of the uncertainty and variability inherent in the health risk estimates that are based on the TEF values assigned by the WHO. During their most recent re-evaluation of the TEF methodology in June 2005, the WHO expressed interest in discussing a probabilistic approach to deriving TEFs for dioxin-like compounds

In a recent publication by Haws and coworkers<sup>2</sup>, the authors presented a refined database of mammalian REPs (relative estimates of potency) for dioxin-like compounds, along with information concerning the distribution of REP values for each congener. However, in developing these distributions, all REPs were treated equally regardless of underlying differences in study quality or relevance. A logical next step in the development of REP distributions is the application of a quantitative weighting scheme to place greater emphasis on those REP values that are of greater quality or are more relevant to humans.

Preliminary REP weighting schemes have been fairly simple, evaluating from 2 to 4 different study factors. For example, Finley et al.<sup>1</sup> developed a weighting scheme based on study type (*in vivo* or *in vitro*) and endpoint using weighting scale based on powers of 10 while Harris et al.<sup>4</sup> developed a weighting scheme based on study type, study duration, multiple versus single dosing, and exposure route using a linear weighting scale.

Another approach for developing REP weighting schemes is to use existing decision analysis methods to develop weights based on multiple decision factors. In this analysis, we will evaluate two decision analysis methods – the Paired Comparison Technique (PCT) described by Dean and Nishry<sup>5</sup> and the Analytical Hierarchy Process (AHP) developed by Saaty.<sup>6</sup> These methods provide an objective framework for aggregating subjective comparisons of the multiple REPs based on a set of decision factors related to REP derivation quality and method. In this analysis we apply these methods to the REP database for PCB 126 based on the work of Haws et al.<sup>7</sup> and compare the weighted distributions generated by them.