

## AN ALTERNATIVE METHOD FOR ESTABLISHING TEFs FOR DIOXIN-LIKE COMPOUNDS. PART 2. DEVELOPMENT OF AN APPROACH TO QUANTITATIVELY WEIGHT THE UNDERLYING POTENCY DATA

Haws LC<sup>1</sup>, DeVito MJ<sup>2</sup>, Birnbaum LS<sup>2</sup>, Walker NJ<sup>3</sup>, Scott PK<sup>4</sup>, Unice KM<sup>4</sup>, Harris MA<sup>5</sup>, Farland WH<sup>6</sup>, Finley BL<sup>7</sup>, and Staskal DF<sup>1</sup>

<sup>1</sup>ChemRisk, Austin, TX; USA, <sup>2</sup>USEPA, ORD, NHEERL, RTP, NC; USA, <sup>3</sup>NIEHS, NIH, RTP, NC; USA, <sup>4</sup>ChemRisk, Pittsburgh, PA; USA, <sup>5</sup>ChemRisk, Houston, TX; USA, <sup>6</sup>USEPA, ORD, Washington, DC; USA, <sup>7</sup>ChemRisk, San Francisco, CA, USA

### Introduction

The current approach for evaluating potential health risks associated with exposure to mixtures of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) [hereafter referred to as "dioxin-like compounds"] is based on the toxic equivalency factor (TEF) methodology. In accordance with this methodology, each PCDD, PCDF, and PCB congener believed to exhibit dioxin-like activity has been assigned a TEF based on comparison to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The current TEFs represent consensus-based values recommended by the World Health Organization (WHO)<sup>1</sup>. In assigning TEFs to each congener, the WHO expert panel employed scientific judgment and a qualitative weighting scheme whereby individual relative estimates of potency (REPs) from *in vivo* studies were given greater weight than *in vitro* studies and/or quantitative structure activity relationship (QSAR) data; chronic studies were given greater weight than subchronic studies, which were given greater weight than subacute studies, which were given more weight than acute studies; and Ah-mediated toxic responses were given more weight than biochemical responses (e.g., enzyme induction)<sup>1</sup>.

The TEF methodology has been re-evaluated in a variety of forums over the past 20 years. Recently, investigators proposed basing risk estimates on the distribution of REP values for each congener to allow for better characterization of the uncertainty and variability inherent in the risk estimates that are based on the TEFs<sup>2,3</sup>. We believe that such an approach is important given that the underlying REPs for most congeners are derived from a heterogeneous data set, and the values themselves often span several orders of magnitude<sup>1,2,4,5</sup>.

Recently, Haws and coworkers published a refined database of REPs and presented distributions of REP values for each congener<sup>3</sup>. However, those distributions were based on treating all REPs equally, despite the many differences between the studies from which the REP values were obtained (e.g., different species, study designs, endpoints, REP calculation methods, etc.). The development of a framework to quantitatively assess differences in study quality and relevance would allow one to place greater emphasis on those REP values believed to be more well-suited for purposes of human risk assessment. In this paper, we present a possible quantitative weighting scheme for consideration.

### Methods

The first step in developing a quantitative weighting scheme involved evaluating different decision analysis methods to identify the most suitable approach for aggregating subjective decision criteria to rank REP values with respect to quality and relevance as described by Scott and coworkers<sup>6</sup>. These authors concluded that the Analytical Hierarchy Process (AHP) was the preferred framework as it can incorporate both multiple value comparison scales (different levels of better or worse) and a binary scale (better or not) and is well documented in the scientific literature. The next step, which is the subject of this paper, involved selecting the specific study elements to include in our quantitative weighting scheme, as well as the specific numerical values that would be applied to each of the study