

ABSTRACT

The ILSI Research Foundation convened a cross-disciplinary working group to examine current approaches for assessing dose-response and identifying safe levels of intake or exposure for four categories of bioactive agents: food allergens, nutrients, pathogenic microorganisms, and environmental chemicals. This effort generated a common analytical framework – the Key Events Dose-Response Framework (KEDRF) – for systematically examining key events that occur between the initial dose of a bioactive agent and the effect of concern. Individual key events are considered with regard to factors that influence the dose-response relationship and factors that underlie variability in that relationship. This approach illuminates the connection between the processes and outcomes occurring at the level of fundamental biology with the outcomes observed at the individual and population levels. Thus, it promotes an evidence-based approach for using mechanistic data to reduce reliance on default assumptions, to quantify variability, and to better characterize biological thresholds. This paper provides an overview of the KEDRF and introduces a series of four companion papers that illustrate initial application of the approach to a range of bioactive agents.

Keywords: low dose dose-response, uncertainty factors, variability, default extrapolation