

Incorporation of global climate change (GCC) effects into regulatory assessments of chemical risk and injury requires an integrated examination of both chemical and non-chemical stressors. Environmental variables altered by GCC, such as temperature, precipitation, salinity and pH, can directly influence toxicokinetics of chemical absorption, distribution, metabolism and excretion, as well as toxicodynamic interactions between chemicals and target molecules. In addition, GCC challenges physiological processes critical for coping with the external environment (water balance, thermoregulation, nutrition, immune-endocrine-neurological systems), leaving some organisms sensitive to even slight perturbations by chemicals when pushed to the limits of their physiological tolerance range. In simplest terms, GCC can make organisms more sensitive to chemical stressors while, alternatively, chemical exposure can make organisms more sensitive to GCC stressors. One challenge is to identify potential interactions between non-chemical and chemical stressors on key physiological processes in an organism. To help achieve this we employed adverse outcome pathways (AOPs), constructs that depict linkages between mechanism-based molecular initiating events and impacts in individuals or populations, to assess how chemical-and climate-specific variables can interact to lead to adverse outcomes. Case examples are presented for scenarios that are prospective, hypothesizing outcomes based on known or anticipated chemical/GCC interactions, as well as retrospective, where mechanisms are proposed for known or demonstrated chemical-climate interactions in natural populations. Understanding GCC interactions along AOPs provides opportunities for extrapolation between species or other levels of organization, development of questions, hypotheses and focal areas for further research, and improved inputs for risk and injury assessments.