

Immunosuppression Guidance Document

The immune system functions as a set of integrated components that act individually or in concert to protect the body against infection by pathogenic organisms and proliferation of neoplastic cells. Conditions, such as exposure to a chemical stressor, that result in diminished function of individual components in the immune system can reduce the ability of the body to ward off infection by pathogens, produce longer and more pronounced manifestations of disease and its sequelae, and increase susceptibility to cancer. As a composite of overlapping and integrated components, the immune system presents a complex setting and requires a more holistic approach to examining how qualitative and quantitative changes in one or more components impact overall immune function.

To address these issues, EPA's Risk Assessment Forum convened a technical panel to develop a guidance document directed at the analysis of immunosuppressive chemicals. The objective of the guidance document is to develop a framework for conducting risk assessments by informing risk assessors of the various components of the immune system and their function with the intent of developing more consistent risk assessments across the agency and improved transparency for stakeholders.

The draft document provides information on the components of the immune system and the implications of immune suppression along with sections on the fundamental components of a risk assessment: hazard identification, dose-response, exposure assessment and risk characterization. Among the topics discussed are how different testing strategies affect the available data base, differences in response across gender and life stages, utility of animal models to human data, dose-response analysis, exposure scenarios, and risk characterization including the relevance of biological significance to statistical significance. The document contains an appendix that covers currently available assays.

This is being brought to the SAB in advance of a future external review.