UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 25 2003

OFFICE OF THE ADMINISTRATOR
SCIENCE POLICY COUNCIL

MEMORANDUM

SUBJECT: Review of the Reference Dose and Reference Concentration Processes

TO: Deputy Administrator
Assistant Administrators
Associate Administrators
Regional Administrators
General Counsel
Science Policy Council

I am pleased to present the EPA's *Review of the Reference Dose and Reference Concentration Processes.* Oral reference doses (RfDs) and inhalation reference concentrations (RfCs) are critical components of the Agency's risk assessments, and these values provide the scientific basis upon which many regulatory actions and program decisions are based. Since the Agency introduced reference values almost 20 years ago, there had not been a comprehensive review of ongoing practice, in particular how well children and other potentially susceptible subpopulations are protected by the Agency's current approach and how thorough current toxicological testing protocols are with respect to life stage assessment, organ systems, and endpoints. With completion of the document, the Agency has taken its first major step toward revising its approach to deriving reference values. This *Review* summarizes current reference value processes, lists recommendations for improvements, and outlines areas that should be explored further. The *Review* is not a guidance, but provides recommendations that should be considered in the development and application of changes to the current RfD/RfC process. The Science Policy Council has accepted the Panel's recommendations, and efforts are currently underway to evaluate their ultimate implementation into Agency practice.

This document results from the work of the RfD/RfC Technical Panel, established by the Risk Assessment Forum in 1999. The Panel represented a broad spectrum of scientific expertise and perspectives across the Agency. This effort was undertaken with knowledge that the RfD/RfC process is a continually evolving process, reflecting the development of the underlying science. The *Review* presents an in-depth discussion of potential areas for improvement in human health risk assessments including the coverage of life stages, assessment endpoints, route, timing and duration of exposure and latency to response. The document also outlines the Panel's suggestions for the incorporation of toxicokinetics and mode of action early in the process. The Panel makes a number of important recommendations, including incorporation of acute, short-term, and longer term reference values in the Integrated Risk Information System (IRIS), where

possible, in addition to chronic reference values. The long-term impacts, nationally and internationally, of this landmark study cannot be overestimated. Implementation of the Panel's recommendations for improvements in the reference value process, along with the future directions identified by the Panel for EPA's research efforts, will have a profound effect on EPA's risk assessments for the foreseeable future.

I encourage Agency personnel to consider this review as we evaluate the recommendations for the RfD/RfC process.

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EPA Science Advisor and
Chair, Science Policy Council

Attachment