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

MAR 2 9 2005

THE ADMINISTRATOR

MEMORANDUM

SUBJECT: Application of New Cancer Guidelines

TO: Assistant Administrators
Regional Administrators
General Counsel
Inspector General
Chief Financial Officer
Associate Administrators
Staff Office Directors

In an effort to update key scientific risk assessment methodologies, the Agency recently finalized its new *Guidelines for Carcinogen Risk Assessment* (Cancer Guidelines) and the related document entitled, *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (Supplemental Guidance). The Cancer Guidelines reflect EPA's evolving approach to cancer risk assessment, resulting from both significant advances in scientific knowledge and the Agency's 20-plus years of experience in applying risk assessment principles and practices. Both the Cancer Guidelines and the Supplemental Guidance reflect the considerable increase in our fundamental understanding of the biological processes of cancer, and are expected to enhance EPA's ability to more accurately assess the carcinogenic potential of environmental contaminants.

EPA began the revision of its 1986 cancer guidelines in light of significant scientific advances in our understanding of the processes of carcinogenesis and the modes of actions of disease at the cellular level. EPA's new Cancer Guidelines set forth recommended principles and procedures to guide EPA scientists in assessing the cancer risks from chemicals or other agents in the environment. They also inform EPA decision makers and the public about these procedures. The Cancer Guidelines are used with other risk assessment guidelines that the Agency has developed, such as guidelines for exposure assessment, in developing an overall characterization of risk to human health. Collectively, all the risk assessment guidelines are intended to promote consistency and technical quality in EPA risk assessments while leaving EPA free to utilize yet-to-be-developed information and procedures. The risk assessment guidelines are meant to be dynamic, flexible documents that would evolve to reflect the current state of the science. In particular, the Cancer Guidelines are intended to promote greater use of the increasing scientific understanding of the mechanisms that underlie the carcinogenic process.

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In the development of the new Cancer Guidelines, several key issues were addressed, including the use of chemical- and site-specific data versus default options, consideration of mode of action and understanding of biological changes, fuller characterization of carcinogenic potential, and consideration of differences in susceptibility.

This memorandum provides implementation direction for the Agency. Effective immediately, the new Cancer Guidelines and Supplemental Guidance will serve as EPA's recommended approach to Agency risk assessors preparing cancer risk assessments. As EPA prepares new cancer assessments under the Integrated Risk Information System (IRIS) program, as well as in other EPA programs, the Cancer Guidelines and Supplemental Guidance will begin to be used as the basis of the Agency's analysis and documentation. Issuance of the Cancer Guidelines and Supplemental Guidance and their potential impact on the analyses contained in the IRIS database will also be taken into account along with other standard selection factors when EPA selects substances for reassessment in annual IRIS agendas (see for example, 70 FR 10616, March 4, 2005). Specifically:

1) For <u>all</u> newly initiated carcinogenicity risk assessments, the Cancer Guidelines and Supplemental Guidance will be used from this point forward.

2) For carcinogenicity risk assessments currently being performed, the Cancer Guidelines and Supplemental Guidance will be used on a case-by-case basis following an evaluation by the Program Office or Region that carefully considers the potential effects of the Cancer Guidelines and Supplemental Guidance on the expected decision and timeline.

3) For risk assessments that have been completed before issuance of the Cancer Guidelines, reassessments may be performed by Program Offices or Regions on a case-by-case basis using the Cancer Guidelines and Supplemental Guidance when a new program-specific or site-specific decision is required that needs to be supported by an updated carcinogenicity risk assessment. Until that time, the current completed assessment will continue to be considered scientifically sound based on the guidance used when the assessment was completed.

If your Program Office or Region has questions or actions regarding implementation, please coordinate with the Science Policy Council's Cancer Guidelines Implementation Workgroup on application of the Cancer Guidelines and Supplemental Guidance until the Agency gains more experience with their use. Please contact either co-chairs, Lee Hofmann in the Office of Solid Waste and Emergency Response at hofmann.lee@epa.gov or Kerry Dearfield in the Office of the Science Advisor at dearfield.kerry@epa.gov, if any assistance is needed.

Stephen L. Johnson
Acting Administrator