

• A novel cumulative risk assessment method, Cumulative Relative Potency Factors, is advanced that integrates the principles of dose addition and response addition to produce multiple-route, chemical mixture risk estimates using total absorbed doses.

The report acknowledges the need for additional research, such as, to conduct a more complete uncertainty and sensitivity analysis on the exposure estimates, and to conduct a more comprehensive analysis of toxic mode of action for the DBPs. This report makes two significant contributions to the science. First, external exposure modeling is conducted and linked with physiologically-based pharmacokinetic modeling to produce internal dose measures of drinking water disinfection by-products (DBPs) for multiple route exposures to be used in mixture risk assessments. Thus, a comprehensive exposure estimate is made for 13 of the major DBPs of concern, including the four trihalomethanes and five haloacetic acids that are currently regulated. Second, a mixtures risk assessment method, based on additivity concepts is proposed to logically evaluate human health risks using total internal doses and oral toxicology dose-response data based on knowledge or assumptions regarding toxic mode of action. This new method is a novel approach to evaluating multiple route exposures that can be generalized for the evaluation of other environmental mixtures.

Dated: December 23, 2003.

Peter W. Preuss,

Director, National Center for Environmental Assessment.

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ENVIRONMENTAL PROTECTION AGENCY

[FRL-7607-8]

Developing Relative Potency Factors for Pesticide Mixtures: Biostatistical Analyses of Joint Dose-Response

AGENCY: Environmental Protection Agency.

ACTION: Notice of availability.

SUMMARY: This notice announces the availability of a final report titled, "Developing Relative Potency Factors for Pesticide Mixtures: Biostatistical Analyses of Joint Dose-Response (EPA/600/R-03-052F)," which was prepared by the U.S. Environmental Protection Agency's (EPA) National Center for Environmental Assessment (NCEA) of

the Office of Research and Development (ORD).

DATES: This document will be available on or about January 7, 2004.

ADDRESSES: The document will be made available electronically through the NCEA Web site (www.epa.gov/ncea). A limited number of paper copies will be available from the EPA's National Service Center for Environmental Publications (NSCEP), P.O. Box 42419, Cincinnati, OH 45242; telephone: 1-800-490-9198 or 513-489-8190; facsimile: 513-489-8695. Please provide your name, your mailing address, the title and the EPA number of the requested publication.

FOR FURTHER INFORMATION CONTACT: The Technical Information Staff, National Center for Environmental Assessment/Cincinnati Office (MS-117), U.S. Environmental Protection Agency, 26 W. Martin Luther King Drive, Cincinnati, OH 45268. Telephone: 513-569-7257; fax: 513-569-7475; e-mail: nceadc.comment@epa.gov.

SUPPLEMENTARY INFORMATION: In 1996, the Food Quality Protection Act and the Safe Drinking Water Act Amendments were passed, each requiring the EPA to consider the risk assessment of chemical mixtures. This report responds to the need for risk assessment research on pesticide mixtures and on chemicals of concern in drinking water. The Relative Potency Factor (RPF) approach is a general methodology for applying dose addition to mixtures of chemicals that produce toxicity by the same toxic mode of action. The current report develops biological concepts and statistical procedures for improving applications of the RPF approach, advancing the theoretical basis for RPF-based risk assessments. New quantitative methods that extend the application of RPFs are shown, addressing the important question of how to assess a mixture containing some chemicals that share a common toxic mode of action and other chemicals that do not. This research was undertaken to continue exploring and developing mixture risk assessment strategies beyond current applications and is intended to enrich the available library of mixture risk assessment methods for future applications of RPF-based risk assessments. This report provides a new set of methods to handle groups of chemicals with more than one toxic mode of action represented. Dose-response modeling techniques are shown, and two algorithms are provided for grouping chemicals into mode of action subclasses that can be modeled with a common slope parameter. The report details approaches to estimate health risks based on the mode of action

subclasses and shows a conceptual approach for estimating a Reference Dose for a mixture using these methods.

Dated: December 23, 2003.

Peter W. Preuss,

Director, National Center for Environmental Assessment.

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ENVIRONMENTAL PROTECTION AGENCY

[FRL-7608-1]

Analysis of Laboratory and Field Studies of Reproductive Toxicity in Birds Exposed to Dioxin-Like Compounds for Use in Ecological Risk Assessment

AGENCY: Environmental Protection Agency.

ACTION: Notice of availability.

SUMMARY: This notice announces the availability of a final report titled, Analysis of Laboratory and Field Studies of Reproductive Toxicity in Birds Exposed to Dioxin-Like Compounds for Use in Ecological Risk Assessment (EPA/600/R-03/114F), which was prepared by the U.S. Environmental Protection Agency's (EPA) National Center for Environmental Assessment (NCEA) of the Office of Research and Development (ORD).

DATES: This document will be available on or about January 7, 2004.

ADDRESSES: The document will be made available electronically through the NCEA Web site (<http://www.epa.gov/ncea>). A limited number of paper copies will be available from the EPA's National Service Center for Environmental Publications (NSCEP), P.O. Box 42419, Cincinnati, OH 45242; telephone: 1-800-490-9198 or 513-489-8190; facsimile: 513-489-8695. Please provide your name, your mailing address, the title and the EPA number of the requested publication.

FOR FURTHER INFORMATION CONTACT: The Technical Information Staff, National Center for Environmental Assessment/Cincinnati Office (MS-117), U.S. Environmental Protection Agency, 26 W. Martin Luther King Drive, Cincinnati, OH 45268. Telephone: 513-569-7257; fax: 513-569-7475; e-mail: nceadc.comment@epa.gov.

SUPPLEMENTARY INFORMATION: Coplanar PCBs and other dioxin-like chemicals are common environmental contaminants and risks to wildlife are a significant issue as demonstrated by