# THE NEED FOR CONTINUED RESEARCH ON DIOXIN AND RELATED COMPOUNDS

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## Introduction

Environmental policy to prevent, eliminate or manage environmental risks is based on a variety of inputs to the decision-making process[1]. Scientific information in the form of a risk characterization is factored in with information on economic, legal, social, political, and engineering considerations to effect "risk management." Risk management policy can range from a decision to take no action at all; to manage risks through a campaign of public information; to institute national or local standards, mandating use of control devices and emission limitations on equipment and facilities; to outright bans on processes or products that are responsible for environmental releases/exposures of chemicals of concern; or to clean-up or regulate access to situations which might represent significant exposure. The process used to organize much of scientific input into the risk management process is called "risk assessment." Risk characterization is the product of the process of risk assessment.

Scientists from the Environmental Protection Agency (EPA), other Federal agencies and the general scientific community have been involved in a comprehensive reassessment of dioxin exposure and human health effects since 1991. The object of this reassessment has been to characterize the potential risks from dioxin exposure, to recognize key assumptions and uncertainties which are integral to this reassessment because of lack of complete information and knowledge, and to identify the research and data collection that will be required to replace assumptions and to reduce uncertainties.

Releases of dioxins to the environment from sources that have been characterized have decreased significantly over the last decade and are expected to continue to decrease. Other sources are still poorly characterized, and an environmental reservoir of dioxins from both man-made and natural sources has been recognized. Human body burdens have also declined, but their relationship to contemporary sources or reservoirs is uncertain.

## Discussion

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (dioxin) is highly toxic to many animal species producing a variety of noncancer and cancer effects. Other 2,3,7,8-substituted polychlorinated dibenzo-*p*-dioxins and dibenzofurans, and coplanar polychlorinated biphenyls (PCBs), exhibit similar effects albeit at different doses and with different degrees of confidence in the database. The similarities in toxicity between species and across different dioxin congeners stem from a common mode of

**[1] The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.**

action via initial binding to the aryl hydrocarbon (Ah) receptor. This common mode of action is supported by consistency in effects evident from multiple congener databases, although uncertainty remains due to data gaps for some congeners. The databases supportive of dioxin-like toxicity, both cancer and noncancer, are strongest for those congeners that are the major contributors to the risk to human populations. This has led to an international scientific consensus that it is prudent science policy to use the concept of toxic equivalency factors (TEFs) to sum the contributions of individual PCDD, PCDF, and coplanar PCB congeners with dioxin-like activity. In addressing receptor-mediated responses resulting from complex mixtures of dioxin-like congeners, this assessment has provided a basis for the use of integrated measures of dose, such as average lifetime body burden, as more appropriate default metrics than average lifetime daily intake. While average body burdens over a lifetime appear to be the most useful dose metric for chronic effects, average body burden during the window of sensitivity may be the most appropriate metric for developmental effects. In fact, the final choice of the appropriate metric may depend on the endpoint under evaluation.

Dioxin and related compounds have been shown in multiple animal species to be developmental, reproductive, immunological, endocrinological and cancer hazards, among others. There is no reason to expect, in general, that humans would not be similarly affected at some dose, and indeed there is a growing body of data supporting this assumption. Based upon the animal data, current margins of exposure are low, especially for more highly exposed human populations. The human database supporting this concern for potential effects near background body burdens is less certain. Occupational and accidentally exposed cohorts exposed at higher levels show correlations with exposure for cancer and a number of noncancer effects, consistent with those seen in the animal studies.

Published results suggest that there was little or no “margin of exposure” just a few years ago and, perhaps, even today. Body burdens in the general population are at or near the concentration where effects might be expected to occur. WHO[2] and other international organizations have concluded that current intakes are “tolerable,” but suggested that all efforts should be made to continue to reduce exposures. However, environmental concentrations and body burdens have been decreasing over the past few decades, from their high in the late 1960s-early 1970s. Only 10 years ago, the estimated average body burden was approximately 10 ng TEQ/kg, as opposed to the data from the present time. The decrease in body burdens is a reflection of the decrease in exposure resulting from a decline in emissions to the environment. Regulation of the major sources of this unwanted contamination in the past, including chlorine bleaching, chlorinated herbicides and biocide production, and incineration, has led to large declines in these sources. Similarly, bans on the production of PCBs has led to decreases in PCB emissions. Thus, the regulatory agendas are successfully reducing many sources and emissions, and, perhaps, exposures to this class of chemicals. While many aspects of the characterization of the health risks of dioxin-like chemicals remains controversial, several international and national advisory groups, including EPA’s own Science Advisory Board[3], have concluded their reviews of dioxin sources, exposure and toxicity with similar recommendations: continue efforts to further reduce exposures and reevaluate the situation periodically as new information becomes available. This seems like prudent advice.

This conclusion, however, suggests a continued importance of dioxin research and data collection

in understanding sources, determining environmental fate and transport and characterizing subtle markers of exposure and response. In addition, research in prevention of formation, pollution control options and pathway interdiction will be needed.

**Summary and Conclusions**

Based on all of the data reviewed in this reassessment and scientific inference, TCDD and related compounds can be characterized as potent toxicants in animals with the potential to produce a spectrum of effects. Some of these effects may be occurring in humans at general population background levels. The potency and fundamental level at which these compounds act on biological systems is analogous to several well-studied hormones. Dioxin and related compounds have the ability to alter the pattern of growth and differentiation of a number of cellular targets by initiating a series of biochemical and biological events resulting in the potential for a spectrum of cancer and non-cancer responses in animals and humans. Despite this potential, there is currently no clear indication of increased disease in the general population attributable to dioxin-like compounds. The lack of a clear indication of disease in the general population should not be considered strong evidence for no effect from exposure to dioxin-like compounds. Rather lack of a clear indication of disease may be a result of the inability of our current data and scientific tools to directly detect effects at these levels of human exposure. Several factors suggest a need to further evaluate the impact of these chemicals on humans at or near current background levels. These are: the weight of the evidence on exposure and effects; an apparent low margin-of-exposure for non-cancer effects; potential for significant risks to some portion of the general population and additivity to background processes related to carcinogenicity in the case of incremental exposures above background.

Given this situation, risk management will continue to be made in the face of these uncertainties. Improvements on the amount and type of information will be required to address these uncertainties. Careful consideration regarding the value of this information vis-à-vis our understanding of risks to public health and the costs and benefits of continuing to reduce human exposure will be required.

**References**

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3. U.S. EPA. (2001) Dioxin Reassessment - An SAB Review of the Office of Research and Development's Reassessment of Dioxin. EPA-SAB-EC-01-006.