

POPULATION VALIDATION EXERCISE OF EPA'S PROPOSED REFERENCE DOSE

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Introduction

In May 2010, the U.S. Environmental Protection Agency (EPA) issued *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*¹. In this document, EPA proposed a Reference Dose for 2,3,7,8-TCDD. This toxicity factor will have major implications for the human health risk assessment of dioxin and furan congeners in all media. It is critical for all organizations, including governmental agencies, to assess the real world implications of their proposed actions to determine if they *make any sense in the context of the real world*. EPA routinely requires that validation exercises be performed whenever a mathematical or biologically-based model is developed. Furthermore, in its Charge to External Reviewers, EPA (2010)² specifically asks the reviewers to comment on whether EPA applied "the epidemiology and animal bioassay study criteria/considerations in a scientifically sound manner." One cannot assess whether EPA's proposed RfD is scientifically sound without performing a real world validation of the resulting toxicological criterion.

Materials and Methods

This paper performs a screening level validation exercise by assessing the implications of the proposed toxicological criterion on the observed health statistics for the US population. Specifically, the proposed RfD is based on a Lowest Observed Adverse Effect Level (LOAEL) of 0.2 ng/kg-day for elevated thyroid stimulating hormone (TSH) levels in neonates³ and decreased sperm count and motility in men exposed to dioxin and furan congeners during childhood⁴.

US population statistics from national databases and published literature with regard to current and historical dioxin and furan serum levels, blood TSH levels, sperm count and sperm mobility have been identified and evaluated. In addition, estimates of current and historical population exposure levels for dioxins and furans from EPA and in the published literature have been identified and evaluated. Deterministic and probabilistic exposure estimates have been made to predict population Hazard Indices assuming the proposed RfD using both thyroid function and sperm abnormalities as endpoints. Population Hazard Indices are then compared to the observed incidence of the endpoints in the population.

Results and Discussion

This paper demonstrates that average TCDD-TEQ exposure levels over time have exceeded the proposed RfD for most, if not all, of the US population, thus predicting that the majority of the population should be experiencing elevated TSH levels and sperm abnormalities (males) if EPA's RfD is a realistic predictor of adverse effects in humans. Population statistics are presented that refute this prediction. In addition, the paper discusses the role of the major etiologic factors that are currently recognized as causal factors for TSH elevations and sperm abnormalities.

This simple screening level population risk assessment used as a validation exercise demonstrates that EPA's proposed RfD for 2,3,7,8-TCDD is not a realistic predictor of human risk and over-predicts the true human risk. It is recommended that the proposed RfD be re-evaluated, and it is recommended that EPA routinely perform a more comprehensive real world validation exercise to assess the reasonableness of any RfD for 2,3,7,8-TCDD before its issuance.

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References

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