USACHPPM
Readiness thru Health
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Just the Facts...

Benchmark Dose Derived Wildlife Toxicity Reference Values in Ecological Risk Assessments

The Benchmark Dose (BMD) approach is used by USACHPPM to derive chemical-specific toxicity reference values (TRVs) for wildlife within Wildlife Toxicity Assessments (WTA; USACHPPM 2000). In WTAs that use the BMD approach, two TRVs are derived: a lower bound on the benchmark dose at the 10 % level (LED_{10}), and the benchmark dose at the 10% effect level (ED_{10}). These values can then be used to estimate risk to ecological receptors using the hazard quotient method. The BMD-derived values are different from the traditional No-Observed-Adverse-Effect-Level (NOAEL) and Lowest-Observed-Adverse-Effect-Level (LOAEL)-based TRVs because they are based on the entire dose-response curve. Because they differ from the conventional NOAEL/LOAEL values, risk assessors may be hesitant to incorporate them in ecological risk assessments. The following information should help ecological risk assessors to understand what the BMD approach values represent and provide justification for their use in ecological risk assessments.

What is a BMD derived TRV?

A BMD derived TRV replaces the typical NOAEL-derived value with one based on a dose-response model that incorporates all relevant data from an important dose-response relationship. The BMD calculates the best fit curve from the dose-response data. It can use incidence data or mean and standard deviation information to derive the values and plot the curve. Each value is based upon the variability of the data.

A BMD is defined as a statistical lower confidence limit on the study dose producing a predetermined level of change in adverse response compared with the response in untreated animals (USEPA 1995). In USACHPPM WTAs, the BMD is reported as the ED_{10}. The second derived value, the benchmark dose-low (BMDL), is defined as the lower 95% confidence interval on the BMD. This value is reported as the LED_{10}. Simply, this means that the LED_{10} is a value where it has been determined that there is a 95% certainty that 10% or fewer organisms would develop the prescribed effect. The ED_{10} represents the exposure where it has been determined that there is a 50% probability that 10% or fewer organisms will develop this prescribed effect. These statistically derived dose-response based values can then be used as the upper and lower bound TRVs in estimating risk to ecological receptors by the hazard quotient method.

Currently, the majority of toxicity reference values for wildlife are based on NOAEL or LOAEL values. The NOAEL value is an experimentally determined exposure level at which there is no statistically or biologically significant increase in the frequency or severity of adverse effects between the exposed population and its appropriate control. Even though most wildlife TRVs were developed from this approach, the NOAEL/LOAEL values have several drawbacks (USEPA 1995). NOAEL/LOAEL-based TRVs are dependent upon the target doses selected in the study, and ignore the dose-response relationships. They also partially consider the variation in the data insofar as the statistical relevance between target doses is concerned. Because of these limitations, the risk assessment community was prompted to develop an alternative method to set standards for noncancer risks (USEPA 1995). The alternative method is the BMD approach.

Why use a BMD derived value?

The BMD approach can be an improved method for TRV derivation provided several objectives are met. However, the BMD approach must be carefully implemented and evaluated. The Benchmark Response (BMR) is the response to toxicant exposure chosen for determination of the BMD. The BMR is the toxicant-induced effect such as growth, behavior, hematological, pathological, and other similar effects.

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The BMD method should only be applied to sublethal responses where the responses fit the BMD mathematical models. A response in 10% of the population is generally the default value for the BMR and is due, in part, to the typical variability in the data and reliability of the model. Once an appropriate BMR is chosen, the BMD is explicitly obtained using mathematical models (see Figure 1). Current guidelines for selection of the BMR are outlined for both quantal data (mortality) and continuous data (body weight) (USEPA 1995).

Considering the above, the selection of the most appropriate data for BMD for determination of a TRV must incorporate professional judgment and a working-knowledge of the principles of risk assessment. USACHPPM WTAs have been through rigorous internal and external review by toxicologists and risk assessors and have incorporated these concerns.

Should an uncertainty factor be applied to BMD values?

Historically, uncertainty factors have been applied to NOAEL/LOAEL TRVs in order to account for uncertainty associated with duration of exposure, inter-species variability and/or other limitations of the available data. In the BMD approach, variability associated with the data design are accommodated by use of the BMDL. However, the BMDL does not account for uncertainties associated with duration of exposure and/or inter-species variability. Current USACHPPM methods (USACHPPM, 2000) include uncertainty associated with exposure duration by focusing on the breadth of the toxicological data. The USACHPPM method avoids the use of uncertainty factors with BMD-derived TRVs since the data used to for the BMD are based on data from the most sensitive species tested.

***Application of BMD values in Ecological Risk Assessment*:**

In ecological risk assessment there is no standard regulatory hierarchy for selecting TRVs. This leaves the selection of each TRV to the risk assessor, in coordination with the regulatory agency. In some cases the BMD derived TRVs may be an order of magnitude lower than the NOAEL from the selected study. Often times risk assessors are reluctant to use a number that is lower (more conservative) than the selected study NOAEL. However, because the BMD uses a statistical approach that incorporates the entire dose-response curve, a BMD value has more certainty associated with it than a NOAEL value, particularly one that has had uncertainty factors applied to it. Therefore, USACHPPM suggests that when risk assessors can select a TRV, they select one based on an appropriately derived BMD. These BMD derived values are considered protective of most mammalian and avian species and are appropriate for screening level risk assessments.

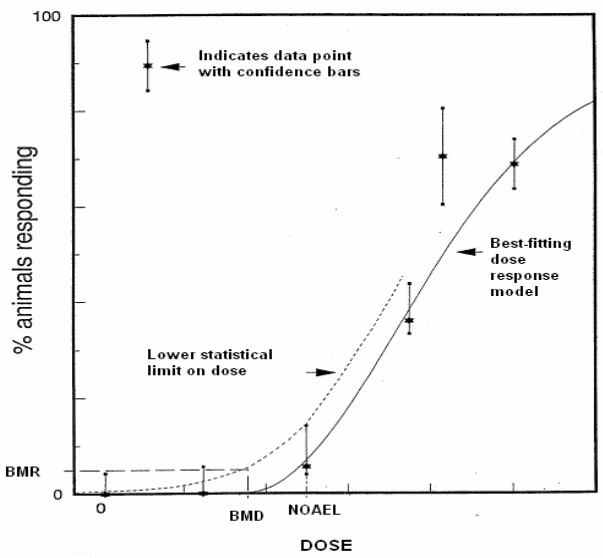

Figure 1. Example of calculation of a BMD

From: USEPA 1995

REFERENCES:

USEPA. 1995. The Use of the Benchmark Dose Approach in Health Risk Assessment. ORD. Washington, DC. EPA/630/R-94/007. February.

U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM). 2000. Standard Practice for Wildlife Toxicity Reference Values, Technical Guide 254.