

Stat 505 - Environmental Statistics - References for part 2  
Analysis of toxicological data

**General Books / Book Chapters**

Finney, D.J. 1971. *Probit Analysis*, 3rd ed. Cambridge University Press.

Finney, D.J. 1978. *Statistical Methods in Biological Assay*, 3rd ed. Griffin and Company.

Both Finney books are classic treatments of the use and interpretation of studies with responses that are yes/no. Overview of the classic methods, usually involving least squares regression on transformed proportions, to estimate dose-response curves. Lots of discussion of concepts, including tolerance distributions.

Gaddum, J.H. 1953. Bioassays and mathematics. *Pharmacological Review* 5:87-134.

Lengthy classic paper on dose-response estimation. Sections on quantal effects apply to our discussions. Quantal responses are responses where you observe yes / no on each individual.

Hosmer, D.W. and Lemeshow, S. 1989. *Applied Logistic Regression* Wiley.

I believe a 2nd ed. is now available. Intermediate level text on logistic regression. Does not discuss overdispersion (at least 1st ed. doesn't).

Kendall, R.J. and Lacher, T.E. Jr. 1994. *Wildlife Toxicology and Population Modeling: Integrated Studies of Agroecosystems* Lewis Publishers.

Papers originally presented at an invited conference on toxicology science and policy. Source of a couple of the assigned readings.

McCulloch, C.E. and Searle, S.R. 2001. *Generalized, Linear, and Mixed Models*. Wiley.

Compact treatment of properties of overdispersed binomial data. My approach to overdispersion based on section 2.6

Morgan, B. J.T. 1996. *Statistics in Toxicology*. Oxford. Univ. Press

## Benchmark Dose and NOEC

Allen, B. C., Kavlock, R.J., Kimmel, C.A. and Faustman, E.M. 1994. Dose-response assessment for developmental toxicity: II. Comparison of generic benchmark dose estimates with NOAELs. *Fundamental and Applied Toxicology* 23:487-495.

Allen, B. C., Kavlock, R.J., Kimmel, C.A. and Faustman, E.M. 1994. Dose-response assessment for developmental toxicity: III. Statistical Models. *Fundamental and Applied Toxicology* 23:496-509.

Crump, K. 1984. A new method for determining allowable daily intakes. *Fundamental and Applied Toxicology* 4: 854-871.

Original paper on the Benchmark Dose method.

Crump, K., Allen B. and Faustman, E. 1995. The Use of the Benchmark Dose Approach in Health Risk Assessment. US EPA, Risk Assessment Forum. EPA/630/R-94/007

Leisenring W, and Ryan L 1992. Statistical properties of the NOAEL. *Regulatory Toxicology and Pharmacology* 15:161-171

Statistical critique of NOEC.

Mantel, N. and Schneiderman, M.A. 1975. Estimating "safe" levels, a hazardous undertaking. *Cancer Research* 35:1379-1386.

West RW, and Kodell RL. 2005. Change-point alternatives to the NOAEL. *Journal of Agricultural Biological and Environmental Statistics* 10:197-211

**Estimating LC<sub>50</sub>** Most of the general books above cover LC<sub>50</sub> estimation in detail.

Hamilton, M.A. 1991. Estimation of the typical lethal dose in acute toxicity studies. pp 61-88 in Krewski, D. and Franklin, C. (eds.) *Statistics in Toxicology*. Gordon Breach Science Publishers.

Stephan, C.E. 1977. Methods for calculating an LC<sub>50</sub>. pp 65-84 in Mayer, F.L. and Hamelink, J.L. (eds.) *Aquatic Toxicology and Hazard Evaluation* ASTM STP 634. American Society for Testing and Materials.

## **Overdispersion**

Kupper, L., Portier, C., Hogan, M., Yamatoto, E. 1986. The impact of litter effects on dose-response modeling in teratology. *Biometrics* 42:85-98.

Ryan, L.M. 1992. Quantitative risk assessment for developmental toxicity. *Biometrics* 48:163-174.

## **Extrapolation to entire communities**

Wagner, C. and Lokke H. 1991. Estimation of ecotoxicological protection levels from NOEC toxicity data. *Water Res.* 25:1237-1242.

Given tox information on a subset of species from a community what can be said about effect on all species?

Smith, E. P. and Cairns, J. Jr. 1993. Extrapolation methods for setting ecological standards for water quality: statistical and ecological concerns. *Ecotoxicology* 2:203-219.

## **Miscellaneous discussions of other issues**

Hothorn, L. A., Lin, K.K., Hamada, C., and Rebel, W. 1997. Recommendations for biostatistics of repeated toxicity studies. *Drug Information Journal* 31: 327-334.

Recommendations from an international consensus committee on studies using repeated doses of toxicant. Concepts, not details.

Krewski, D., Leroux, B.G., and Zhu, Y. 1996. Statistical analysis of toxicological experiments on carcinogenicity, mutagenicity, and developmental toxicity. Chapter 21 in Armitage, P. and David, H.A. *Advances in Biometry*. New York: Wiley

Review of a very extensive literature. Each of the three sections (on carcinogenicity, mutagenicity, and dev. tox. presents mathematical models, trend tests (does response increase with dose) and dose-response models.

Mudholkar, G.S. and George, E.O. 1978. A remark on the shape of the logistic distribution. *Biometrika* 65:667-8