Summary of Changes to the Dose-Response Modeling

Since the December 2001 publication of the Preliminary Analysis, the inability to fit more datasets with the expanded model prompted a reexamination of both the basic and expanded models. The resulting analyses and small changes in RPFs will be discussed in more detail in the February meeting of the FIFRA SAP.

1) Reparameterization of Basic and Expanded Models

The difficulty in fitting the expanded model caused a reexamination of the models used. In the parametrization used in the Preliminary Analysis (December 2001), the parameters m (slope scale factor) and P_B (horizontal asymptote) were highly correlated. In marginal datasets, this could cause a complete failure to estimate all the parameters, or, in less severe cases, could result in somewhat less than optimal estimates being returned. Reparameterizing the basic and expanded models in terms of *BMD* (benchmark dose) instead of *m,* as was described in the technical appendix (III.B.1), considerably reduces this correlation. Profile likelihoods for P_B have been recomputed using this alternative parameterization and will available at the February 5-8, 2002 meeting of the FIFRA SAP.

2) Sensitivity Analyses

The sensitivity of estimates of *BMD* to different characterizations of the random and fixed effects models, and to different plausible values for P_B when it is not directly estimable, has been evaluated. The sensitivity analysis has shown that when it was not possible to estimate P_B it was because of the experimental designs used, specifically, that the highest dose used was not high enough to allow precise estimation of P_B.

3) Programming Errors in R Code

The programming code released in the Preliminary Cumulative Risk Assessment (III.B.4) includes two programming errors. These programming errors impact the computation of the SD profiles. One of these errors is responsible for the inability to estimate the SD profile when that estimation failed. This error has been corrected.

The other error caused profile likelihood plots (for S and D only) to have incorrect axis labels, and the incorrect initial guesses for these parameter values to be read off the graphs. As of 1/22/2002, this error was corrected and recalculation of S and D was on-going. Revised SD profiles will be available for the February 5-8, 2002 SAP meeting.