March 4, 2002

IUL Study Plan Questions

1. EPA views the IUL assay primarily as a potential substitute for a full Tier 2 study when only endocrine sensitive endpoints need to be examined (i.e., when valid data from a 2-generation study exist). The other potential use includes substitution for all mammalian in vivo assays in Tier 1 (pubertal assay, uterotrophic and Hershberger. Is the initial study design, breaking the study into three cohorts (uterotrophic with 1 female per litter, pubertal female with 4 females per litter, and pubertal male), consistent with these purposes?

2. Are the endpoints for each of the cohorts appropriate to the design of the study?

3. Is the rationale clear as to why the pubertal cohorts are further subdivided into dosed and undosed groups? Will this design result in sufficient power in the test to detect the endpoints of interest? Do you agree with this design as being appropriate for a test and/or a screen?

4. Does the EDMVS agree with the conduct of a demonstration study using one chemical? Do you agree with methoxychlor as the choice for that chemical?

5. Are the choices of doses (0, 25, 50, 100 mg/kg/day MXC in corn oil to the dams, and pubertal cohorts and the same administered sc to the utertrophic cohort) appropriate? Are the dosing periods appropriate?

6. Do you agree with the data collection and analysis procedures recommended in the protocol?