

Pubertal assays: Questions for EDMVS
December 2001

Single-dose study

1. This study was conducted in two strains of rats. Given the later onset of preputial separation (PPS) and the greater variance associated with the mean age of PPS in the Long-Evans strain in this study, does EDMVS agree that the pubertal protocol should be standardized using the Sprague-Dawley strain? Should EDSP attempt to define strain differences, and if so, at what point in the validation process should this occur?

Multiple-dose study

1. The purpose of this study is to examine lower limits of detection of the pubertal assay. Does EDMVS agree that vinclozolin is an appropriate chemical to use in the male pubertal assay, and that methoxychlor is an appropriate chemical for the female pubertal assay, for this purpose?
2. As a result of difficulties encountered in the single-dose study, additional descriptive text was added to the Work Assignment for this study (not distributed to EDMVS but fully reflected in the protocols) drawing attention to the care with which small organ weights must be taken to avoid excessive variability due to dessication and other procedural variations during necropsy. In addition, EPA requested a demonstration of necropsy technique in the single dose study and the array study to ensure that data reflect the full capabilities of the assay rather than limitations of technique. Finally, EDSTAC has recommended that positive controls be included in each study to ensure that the assays are performed correctly. Does EDMVS have any recommendations on how to ensure accuracy of the results for this assay, which includes endpoints that have heretofore not been frequently used?

Array study

1. Do the chemicals chosen for this study adequately cover the range of mechanisms that should be examined?
2. In contrast to the multiple-dose study, organ weights for liver, kidneys, pituitary, and adrenal glands will be taken in this study only if warranted. Does the EDMVS agree that these particular organ weights should be optional endpoints in the pubertal assays, or should they be required?

(Note: weights of testes, epididymides, prostate, seminal vesicles with coagulating gland, levator ani/bulbocavernosus muscle complex, thyroid, and uterus are required, not optional, endpoints.)