

Questions for the EDMVAC
on the pubertal interlaboratory validation study
April 19, 2006

The purpose of the interlaboratory validation study was to evaluate whether, when using these assays, different contract laboratories produce similar results when testing the same chemicals at the same dose levels. Results are considered “similar” for the purposes of Tier-1 screening for endocrine disruption if the weight of evidence from all endpoints in the assay leads to the same conclusion from each laboratory concerning whether the chemical has the potential to interact with the endocrine system.¹

Questions:

1. Did this study demonstrate that similar results are obtained across laboratories in the male pubertal assay? the female pubertal assay?
2. Are the performance criteria, based on coefficients of variation for control animals, adequate indicators of a laboratory’s ability to perform the assay correctly? If the criteria are adequate, could they be made more efficient? If the criteria are not adequate, how could they be made adequate?
3. Should certain endpoints be weighted more heavily than others in weight-of-evidence determinations? If so, which endpoints, and why?
4. Should any endpoints be dropped from the assay? More specifically, would there be significant increases in efficiency (value of information divided by the cost of obtaining that information) if certain endpoints were dropped from the assay?

¹ EPA is not requiring that the assay consistently display a pattern of endpoint responses diagnostic for a particular mode or mechanism of action (e.g., estrogenicity, anti-estrogenicity, androgenicity, anti-androgenicity, interference with receptor binding, interference with the steroidogenesis pathway), but only that thyroid-associated responses not be used to claim consistency with sex-steroid-associated responses or vice versa. In addition, EPA recognizes that a decision about whether there is the potential for interaction of a test chemical with the endocrine system is likely to be based on results from a battery of assays, not on any assay in isolation. Nevertheless, for reasons of practicality, EPA has chosen to validate individual assays separately, prior to validation of whatever battery is finally chosen. This necessitates an evaluation of the pubertal assay(s) as if no other information were available for the decision on whether there is an interaction with the endocrine system.