

EPA's Endocrine Disruptor Methods Validation Advisory Committee (EDMVAC)

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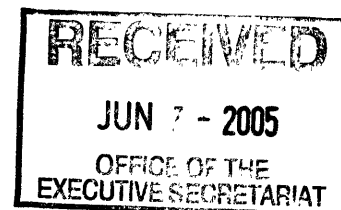
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May 3, 2005

Stephen L. Johnson, Administrator
United States Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460



Re: EDMVAC consensus recommendation on the continued development
of the sliced testis steroidogenesis assay

Dear Administrator Johnson:

The Endocrine Disruptor Methods Validation Advisory Committee (EDMVAC) is providing guidance and scientific counsel to the US EPA along the path to regulatory implementation of a screening and testing program to assess the endocrine-disrupting properties of chemicals. This screening and testing program is mandated under the Food Quality Protection Act of 1996. Among the current tasks of the EDMVAC, is providing guidance to ensure a scientifically-defensible validation process for several candidate screening assays.

The EDMVAC was apprised of the status of the "sliced testis steroidogenesis assay" at its April 2005 meeting. This assay is designed to detect the ability of chemicals to interfere with the testosterone biosynthetic pathway. Pre-validation experiments performed using the protocol, as previously developed, and demonstrated that the assay was capable of detecting the steroidogenic effects of chemicals that are known to disrupt this pathway. However, the limited ability of the assay to readily discern specific endocrine toxicity from overt cell toxicity greatly reduced the enthusiasm of the Committee towards this assay. The Committee viewed this apparent inability to discern specific toxicity as a potentially fatal flaw in the assay when evaluating chemicals having unknown toxicological properties.

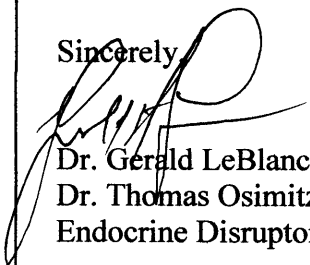
The following consensus view was reached by the Committee:

The sliced testis steroidogenesis assay, in its current form, is inadequate in its ability to discern specific effects of chemicals on the steroidogenic pathway associated with Leydig cells from overt toxicity to the cellular milieu of the testicular tissue. The Committee recommends that the US EPA:

- a) cease, at least temporarily, efforts to validate this assay;
- b) investigate improved methods to detect overt cellular toxicity that could be readily incorporated into the assay to improve its specificity;
- c) direct resources towards the identification and development of alternative screening approaches – that would more likely withstand the rigors of validation – to detect chemicals that disrupt steroidogenesis.

The Committee views the cell-based H295R assay, which is also under development as a potential screening assay, as having significantly greater promise over the sliced testis steroidogenesis assay.

Sincerely,



Dr. Gerald LeBlanc, Chair
Dr. Thomas Osimitz, Co-Chair
Endocrine Disruptors Methods Validation Advisory Committee

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