



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON D.C., 20460

OFFICE OF  
PREVENTION, PESTICIDES, AND  
TOXIC SUBSTANCES

**MEMORANDUM**

**DATE:** March 13, 2008

**SUBJECT:** Transmission of Revised Charge Questions for the March 25-28, 2008 Session of the FIFRA Scientific Advisory Panel (SAP) Entitled "Review the Endocrine Disruptor Screening Program (EDSP) Proposed Tier-1 Screening Battery"

**FROM:** Linda J. Phillips, Director *Linda Phillips*  
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**TO:** Jim Downing, Designated Federal Official  
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The questions listed below are a set of revised Charge Questions for the March 25-28, 2008 Session of the FIFRA Scientific Advisory Panel (SAP) Entitled "Review the Endocrine Disruptor Screening Program (EDSP) Proposed Tier-1 Screening Battery." Please replace the SAP Charge Questions with these questions:

1. Please comment on the ability of the proposed Tier 1 screening battery to provide sufficient information to determine whether or not a substance potentially interacts with the estrogen, androgen, and thyroid hormonal systems based on the modes of action covered within the battery:
  - a. Estrogenicity: acting agonistically by potentiating the estrogen signal
  - b. Anti-estrogenicity: acting antagonistically by attenuating the estrogen signal
  - c. Androgenicity: acting agonistically by potentiating the androgen signal
  - d. Anti-androgenicity: acting antagonistically by attenuating the androgen signal
  - e. Steroidogenesis effects: modulating normal steroidogenic processes including aromatase by inducing or inhibiting enzymes in the sex steroid hormone synthesis pathway

- f. Hypothalamic/pituitary/gonadal effects: interference with the hypothalamic-pituitary regulation of gonadal function including the production of hormones and gametes.
  - g. Hypothalamic/pituitary/thyroid effects: modulation of the processes associated with direct thyroid hormone receptor interaction as well as those processes involved indirectly (e.g., synthesis, secretion, elimination of thyroid hormones) in thyroid function.
2. EPA proposed a Tier 1 screening battery that includes many assays that are complementary in nature in their coverage of the EAT hormonal systems (the strengths of one assay offset the limitations of another), albeit by different taxa, life-stages, endpoints, exposure and use of *in vitro* and *in vivo* methods executed at different levels of biological organization (e.g., cytosolic receptor binding, cell-based assays, whole organism).
- a. Please comment on how well the proposed battery minimizes the potential for “false negatives” and “false positives.”
  - b. Are there any unnecessary redundancies for MOAs across the battery?
  - c. Please comment on whether a different combination of validated assays would be more effective in achieving the purpose of the battery than that proposed by EPA.