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

OFFICE OF
CHIEF FINANCIAL OFFICER

May 15, 2002

The Honorable Christopher Bond
Ranking Member, Subcommittee on VA,
HUD and Independent Agencies
Committee on Appropriations
United States Senate
Washington, DC 20510

Dear Senator Bond:

I am pleased to submit for your review the Environmental Protection Agency's report on the status of the Endocrine Disruptor Methods Validation Subcommittee (EDMVS) as required by the FY 2002 VA/HUD and Independent Agencies Appropriation committee (H. Rpt. 107-159, p.60) and the FY 2002 Conference Report 107-272, pg. 133. The report provides an update on the progress of the Agency's Endocrine Disruptor Methods Screening program and describes validation processes that incorporate the advice of the EDMVS. It also includes summaries of recent subcommittee meetings and a list of subcommittee members. I trust you will find the report responsive to your needs.

Should you have any questions or need additional information, please contact me at (202) 564-9673, or Nanci Gelb, Director of the Annual Planning and Budget Division, at (202) 564-8340.

Sincerely,

/s/

Joseph L. Dillon
Comptroller

Enclosure

March 2002

Report to the U. S. House of Representatives Committee on Appropriations on the Status of the Endocrine Disruptor Methods Validation Subcommittee

The U.S. Environmental Protection Agency (EPA) respectfully submits this report regarding the status of the Endocrine Disruptor Methods Validation Subcommittee (EDMVS) to the U.S. House of Representatives Committee on Appropriations. This report is submitted in response to Conference Report 107-272 accompanying H.R. 2620 requesting that EPA provide a status report on the EDMVS to the Committee by March 15, 2002.

To date, there have been two full meetings of the 26-member EDMVS. The EDMVS has provided useful input for addressing the difficult issues facing EPA's Endocrine Disruptor Screening Program. EPA is developing validation processes that incorporate the advice of the EDMVS. Robust discussions of the EDMVS have helped to establish promising methodologies for predicting endocrine disruption potential, as well as for reducing the numbers of animals that will be required for these tests. As envisioned, the EDMVS is providing a means by which interested parties can participate to express their concerns and work to ensure that scientifically-sound validation processes are developed for animal and non-animal based screens and tests. These screens and tests are now undergoing the rigorous process of protocol review, pre-validation and validation.

Background

In 1996, through enactment of the Food Quality Protection Act, which amended the Federal Food, Drug, and Cosmetic Act, Congress directed the Environmental Protection Agency (EPA) to develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have hormonal effects in humans. In October 1996, EPA chartered a scientific advisory committee– the Endocrine Distruptor Screening and Testing Advisory Committee (EDSTAC)–under the authority of the Federal Advisory Committee Act (FACA) to advise it on establishing a program to carry out Congress' directive. EDSTAC recommended a multi-step approach–including a series of screens (Tier 1 Screens) and tests (Tier 2 Tests)–for determining whether a chemical substance may have an effect similar to that produced by naturally occurring hormones. In order to carry out Congress' directive, EDSTAC's recommendations were utilized by EPA as a foundation for the development of the Endocrine Disruptor Screening Program (EDSP).

EDSTAC also recognized that there currently are no validated test systems for determining whether a chemical may have an effect in humans that is similar to an effect produced by naturally occurring hormones. Consequently, EPA is in the process of developing and validating the screens and tests that EDSTAC recommended for inclusion in the EDSP. In carrying out this validation exercise, EPA is working closely with, and adhering to the principles of the Interagency Coordinating Committee for the Validation of Alternate Methods (ICCVAM). EPA also is working closely with the Organization for Economic Cooperation and Development's Endocrine Disruptor Testing and Assessment work group to validate and harmonize endocrine screening tests of international interest.

Finally, to ensure that EPA has the best and most up-to-date advice available regarding the validation of the screens and tests in the EDSP, EPA recently chartered the Endocrine Disruptor Methods Validation Subcommittee (EDMVS) of the National Advisory Council for Environmental Policy and Technology (NACEPT). EDMVS provides independent advice and counsel to the Agency through NACEPT, on scientific and technical issues related to validation of the EDSP Tier I and Tier II assays, including advice on methods for reducing animal use, refining procedures involving animals to make them less stressful, and replacing animals where scientifically appropriate.

Status of the Endocrine Disruptor Methods Validation Subcommittee

Formation of the EDMVS and Selection of Members

On May 7, 2001, the Agency published a notice in the Federal Register requesting from interested organizations nominations for members to serve on the EDMVS (66 FR 23022). By June 6, 2001 (the designated closing date of the nominations process), EPA had received approximately 50 nominations from many sectors and international interests.

EPA selected members of the EDMVS on the basis of their relevant scientific expertise and diversity of perspectives on (1) mammalian, ecological, and in vitro endocrine disruptor screening and testing methods and procedures; (2) toxicity test methods standardization and validation; and (3) the chemical and pesticide regulatory processes. EDMVS members selected represent a balance of the following sectors: the agrichemical and commodity chemical industries; environmental organizations; public health organizations; academia; animal welfare organizations; Federal Agencies; and State governments. These nominees were notified by September 7, 2001. A list of the 26 selected EDMVS members and their expertise is attached (Attachment A).

Mission

EDMVS is to provide advice and counsel to the EPA on scientific issues associated with the conduct of studies necessary for validation of Tier I and Tier II assays for the EPA's Endocrine Disruptor Screening Program (EDSP) including the reduction of animal use, refining procedures involving animals to make them less stressful, and replacing animals where scientifically appropriate. The EDMVS will provide advice and recommendations regarding : the development and choice of initial protocols; pre-validation study designs; validation study designs; and the integration of pre-validation and validation study results into EDSP Tier1 and Tier II methods documents suitable for external peer review. The EDMVS advice and recommendations will be forwarded to the Agency through NACEPT. Taking into account this advice and recommendations, the EPA will coordinate the management and implementation of pre-validation and validation laboratory studies in cooperation with the Interagency Coordinating Committee for the Validation of Alternate Methods (ICCVAM) and the Organization for Economic Cooperation and Development (OECD).

First Meeting of EDMVS- October 30-31, 2001

Meetings of the EDMVS are currently being scheduled every 3 to 4 months. The first meeting of the EDMVS was held on October 30-31, 2001 in the Washington, D.C. area (Attachment B). The purpose of this meeting was to present to the members of this newly established federal advisory committee:

- an overview of the EPA's Endocrine Disruptor Screening Program;
- develop a clear understanding of the EDMVS scope, purpose, and operating procedures;
- provide background information on test protocol validation and approaches;
- discuss Interagency Coordination Committee on the Validation of Alternative Methods (ICCVAM) test protocol validation process;
- EDSP's approaches to test protocol validation and process: Relationships between ICCVAM, Organisation for Economic Co-operation and Development (OECD), EPA and EDMVS;
- EDSP's test protocol validation status / timeline; and
- OECD's test protocol validation process by illustration of the uterotrophic assay.

Second Meeting of EDMVS - December 10-12, 2001

The second meeting of the EDMVS was held December 10-12, 2001, in Washington, D.C (Attachment C). The purpose of this meeting was to reach final agreement on the EDMVS mission statement and work plan, and to provide advice on the pre-validation of three assays/tests:

Tier I screening

- the pubertal assay study designs for the multi-dose and chemical array protocols;
- the *in utero* through lactation assay (alternative);

Tier II test

- the mammalian 2- generation reproduction study with the extended one generation design.

Future Meetings

Upcoming meetings of the EDMVS are scheduled for March 25-27, June 10-12, and tentatively for September 2002 and December 2002 depending on the progress of the assays through pre-validation and validation in the laboratory. The EDMVS has a substantial work load for these and future meetings which will include reviewing pre-validation and validation reports for all the assays/tests listed below and additional some will require protocol review, as well:

Tier I screens

- frog thyroid screening assay
- fish reproduction screening assay
- steroidogenesis screening assay
- pubertal female screening assay
- pubertal male screening assay (alternative Tier I)
- aromatase (alternative Tier I)
- in utero through lactation assay (alternative Tier I / II)

Tier II tests

- fish chronic and partial life cycle assay
- avian assay
- mammalian 2-generation assay
- amphibian assay
- invertebrate assay

Tentative Schedule for Future Meetings

March 25-27, 2002
June 10-12, 2002
September 2002
December 2002
Spring/Summer/ Fall/Winter 2003

In 2004, the EPA will then be seeking advice from the EDMVS on the assay composition of the Tier I screening battery.

To date, the EDMVS has provided useful input for addressing the difficult issues facing EPA's Endocrine Disruptor Screening Program. EPA is developing validation processes that incorporate the advice of the EDMVS. Robust discussions of the EDMVS have helped to establish promising methodologies for predicting endocrine disruption potential, as well as for reducing the numbers of animals that will be required for these tests. As envisioned, the EDMVS is providing a means by which interested parties can participate to express their concerns and work to ensure that scientifically-sound validation processes are developed for animal and non-animal based screens and tests. These screens and tests are now undergoing the rigorous process of protocol review, pre-validation and validation. Please visit the EDMVS website for more detailed information about individual tests at (http://www.epa.gov/scipoly/oscpendo/edmvs.htm).