May 2, 2008

Dr. George Gray
Assistant Administrator
Office of Research and Development
U.S. Environmental Protection Agency
Washington, D.C. 20460

Dear Dr. Gray:

The Board of Scientific Counselors (BOSC) has completed a Mid-Cycle Review of ORD's Endocrine Disrupting Chemicals Research Program (EDCRP). This review focuses on the Agency's efforts and progress following a detailed BOSC subcommittee review of the EDCRP conducted in 2004 and subsequent BOSC report provided to ORD in April 2005. Drawing from the original review subcommittee, a four-member BOSC subcommittee (including one new member) was charged to conduct the mid-cycle review. The Subcommittee was chaired by Dr. Deborah Swackhamer, a member of the BOSC Executive Committee. The Subcommittee conducted teleconference review of ORD provided information and presentation materials in the fall of 2007 with a face-to-face meeting with EDCRP researchers and management in September 2007. The Mid-Cycle report was delivered for BOSC Executive Committee approval in April 2008. This report has been vetted by the BOSC and appropriately clarified, revised, and approved for transmittal to ORD.

The purpose of the mid-cycle review is to provide general feedback on ORD's progress to date and, as appropriate, responsiveness to previous BOSC recommendations to assist in addressing issues and opportunities surrounding continued development of the Endocrine Disrupting Chemicals Research Program's Multi-Year Plan. Specific charge questions guided the BOSC Subcommittee in accomplishing the analysis of the materials prepared for the review process and in preparing the final report itself. Each of the charge questions has been addressed by detailed response in the BOSC Subcommittee review.

The summary findings of the mid-cycle review point to a program that exceeds expectations in progress to address concerns of the previous 2004 program review. The EDCRP provides a logical and structured multi-year planning framework for identifying priority research to meet regulatory

mandates. The EDCRP has taken under consideration all recommendations of the previous BOSC review and those recommendations not implemented were held in abeyance because of budgetary constraints.

This report is anticipated to further assist ORD in longer term program enhancement, comparative analysis with other programs, and intermediate research investment decision-making. We expect the report will assist ORD in continuing to improve its science, and assist and inform clients within and outside the EPA of the significance of its research and its utilization. On behalf of the BOSC Executive Committee and the EDCRP Subcommittee it is my pleasure to transmit this mid-cycle report to ORD.

Although the BOSC welcomes any response to the report; the Subcommittee finds and the Executive Committee concurs that a formal response to the report is not required by the EDCRP. Please feel free to contact me if you have any questions concerning this report.

Sincerely,

Gary S. Sayler
Chair

B·O·S·C

BOARD OF SCIENTIFIC COUNSELORS

MID-CYCLE REVIEW OF THE OFFICE OF RESEARCH AND DEVELOPMENT'S ENDOCRINE DISRUPTING CHEMICALS (EDCS) RESEARCH PROGRAM AT THE U.S. ENVIRONMENTAL PROTECTION AGENCY

BOSC MID-CYCLE SUBCOMMITTEE ON ENDOCRINE DISRUPTING CHEMICALS (EDCS) RESEARCH

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April 16, 2008

This report was written by the Endocrine Disrupting Chemicals (EDCs) Mid-Cycle Subcommittee of the Board of Scientific Counselors, a public advisory committee chartered under the Federal Advisory Committee Act (FACA) that provides external advice, information, and recommendations to the Office of Research and Development (ORD). This report has not been reviewed for approval by the U.S. Environmental Protection Agency (EPA), and therefore, the report's contents and recommendations do not necessarily represent the views and policies of the EPA, or other agencies of the federal government. Further, the content of this report does not represent information approved or disseminated by EPA, and, consequently, it is not subject to EPA's Data Quality Guidelines. Mention of trade names or commercial products does not constitute a recommendation for use. Reports of the Board of Scientific Counselors are posted on the Internet at http://www.epa.gov/osp/bosc.

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I. SUMMARY

A Board of Scientific Counselors (BOSC) Subcommittee of four members conducted a mid-cycle review of the U.S. Environmental Protection Agency's (EPA) Endocrine Disruptors Research Program (EDRP) from September to November 2007. This review included three conference calls and one face-to-face meeting. This review was conducted to evaluate the response of the ERDP to the BOSC program review that took place in 2004, and to offer advice and feedback with regard to future program directions.

EPA's Office of Research and Development (ORD) charged the Subcommittee to address the program's response to the 2004 review and the adequacy of the updated Multi-Year Plan (MYP). The Subcommittee also was asked for an assessment of specific performance metrics for the program, and advice on the future directions of the program given its evolution and budget constraints. In addition, the Subcommittee was asked to rate the progress of the program using the BOSC qualitative scoring tool, assigning a score of exceptional, exceeds expectations, meets expectations, or not satisfactory.

The Subcommittee concluded that the EDRP has been very responsive to the recommendations of the 2004 BOSC program review. The EDRP has considered the recommendations and implemented most of them. In cases where the EDRP did not implement the recommendations, it was almost exclusively because of budget constraints. To the program's credit, the EDRP continues to support science that will reduce the uncertainty regarding endocrine disrupting chemicals (EDCs) and provide EPA with a sound scientific background for environmental decision-making. The Subcommittee notes that EPA has been a leader in the development of genomics, proteomics, metabolomics, computational modeling, and whole animal endpoints to identify biomarkers of exposure to EDCs. In response to recommendations made by the BOSC in its 2004 program review, the EDRP has partnered extensively with other agencies with interests in EDCs. One of the most difficult and expensive challenges has been the epidemiologic studies that have produced some results and have received funding from other agencies. This is not a traditional strength for EPA and, because of limited resources, support for epidemiology must continue to be done in partnership with other agencies. The BOSC also recommended that EPA investigate the integration of ecological and human health risk assessment. Owing to budget constraints, there has been only modest progress in addressing this recommendation. Finally, the EDRP has made significant progress in completing the research needed to develop and standardize assays for the Agency's Endocrine Disruptor Screening Program (EDSP).

The Subcommittee found that the updated draft MYP is very logical, and provides a coherent framework and rational for addressing priority research needs of the EDRP.

The Subcommittee members thought that the metrics being used to assess progress are appropriate, and recommended that quantitative metrics to assess the impact of the science on the advancement of the field, policy, regulation, and decision-making also be included. Metrics that

assess the level of collaboration within the Agency as well as with other federal, industry, and academic partners, also should be developed.

The Subcommittee did not identify any obvious research gaps or needs not already acknowledged by the program, and encourages the EDRP to continue to develop and improve ongoing programs. The Subcommittee recognized that the EPA has achieved significant leadership in EDC research and encourages the program to further enhance the Agency's leadership role in the area of risk management.

The Subcommittee rated the overall progress of the EDRP program as *Exceeds Expectations.* This program has established itself as a leader in several areas of EDC research. It has leveraged expertise across the Agency and with other federal and academic scientists; it has been quick to respond and adapt its focus and research questions to the rapidly changing research landscape of EDCs; and it has developed an excellent new MYP. The EDRP has accomplished a remarkable amount in the face of diminishing financial resources. Because the program is progressing well, there is no need for ORD to respond to this review.

II. INTRODUCTION

The U.S. Environmental Protection Agency's (EPA) Office of Research and Development (ORD) enlists the Board of Scientific Counselors (BOSC) to conduct independent expert reviews of ORD's environmental research programs every 4 to 5 years. Mid-cycle reviews, scheduled midway through the review cycle, are a critical step in this process. Narrower in focus than the in-depth technical evaluation that constitutes a full program review, the objectives of a mid-cycle review are to gauge the program's progress and to offer advice and feedback with respect to future direction and performance and accountability.

An eight-member BOSC subcommittee completed a full program review of the Endocrine Disruptors Research Program (EDRP) during an open meeting held in Research Triangle Park, North Carolina, on December 13-15, 2004. This culminated in a BOSC report that was transmitted to ORD on April 21, 2005. The ORD response to the report was transmitted to the BOSC on September 8, 2005.

Three of the members of the original subcommittee that conducted the 2004 BOSC program review served on the Endocrine Disruptors Research Mid-Cycle Review Subcommittee that was enlisted to conduct the mid-cycle progress review. This Subcommittee included one additional member who had not served on the 2004 program review subcommittee. The Endocrine Disruptors Research Mid-Cycle Review Subcommittee had one organizational telephone conference, followed by an open face-to-face meeting held in Arlington, Virginia on September 18, 2007. Two subsequent conference calls took place on October 17, 2007 and November 6, 2007. In addition to the 2004 BOSC program review and the ORD response to that review, the EDRP provided the Mid-Cycle Subcommittee with a Progress Report (September 2007), the draft Multi-Year Plan (MYP), the annual performance goals, a bibliometric analysis, program performance measures and goals, a bibliography, and a synthesis of research. Program staff also presented much of this material in a series of Power Point presentations. Following the face-to-face meeting, a draft report was prepared by the Subcommittee and submitted to the BOSC Executive Committee for review and approval in January 2008.

ORD requested that the Subcommittee address the following charge questions in its mid-cycle review:

- **Charge Question #1:** How responsive has the Endocrine Disruptors Research Program been to the recommendations from the 2004 BOSC program review?

- **Charge Question #2:** To what extent does the updated draft MYP provide a coherent framework and rationale for addressing priority research needs?

- **Charge Question #3:** Are there performance metrics the Endocrine Disruptors Research Program should be using in addition to the current indicators (e.g., quality and impact of ORD publications, timeliness of completing goals) for regularly assessing research

progress?

- **Charge Question #4:** What advice can the BOSC provide regarding the planned narrower focus and directions of the Endocrine Disruptors Research Program given its evolution and budget impacts?

- **Charge Question #5:** Please rate the progress made by the Endocrine Disruptors Research Program in moving the program forward in response to the BOSC program review of 2004 by assigning a qualitative score, i.e., exceptional, exceeds expectations, meets expectations, or not satisfactory.

III. RESPONSES TO CHARGE QUESTIONS

A. Charge Question #1

How responsive has the Endocrine Disruptors Research Program been to the recommendations from the 2004 BOSC program review?

The EDRP has been very responsive to the recommendations of the 2004 program review. This is reflected in a comprehensive narrative that was provided initially in ORD's 2005 response to the comments of the program review (Report by Elaine Francis dated September 8, 2005) and subsequently in the September 18, 2007 background materials prepared for the 2007 mid-cycle review prepared by ORD's EDRP Planning Team. The EDRP provided a thorough and well-thought out response to each recommendation, as well as specific details on the current stage of implementation of the response. This was exceptionally helpful to the Subcommittee in answering this charge question, but more importantly, it required the EDRP to carefully consider its initial responses to the recommendations and articulate a response.

Despite the priority the Agency has placed on EDC research, the budget to support this program has been cut substantially. The budget has been cut 20 percent since 2003, with a 4 percent cut proposed for this year. Funds for extramural STAR grants for EDC research were completely eliminated in 2005. This has required a refocus of the EDRP priorities and a downsizing of the program objectives. In some cases, where a recommendation was not possible to implement, the program has been creative in trying to meet the intent of the recommendation.

One of the overarching recommendations of the 2004 BOSC program review was for the EDRP to enhance the research expertise that participates in the program. Given budgetary constraints, the EDRP has showed sound management in building its work force and fostering new partnerships that enhance its research base as well as strengthen the program. For example, given the limited resources to hire new permanent EPA staff, the EDRP has leveraged its in-house staff with postdocs, fellows, graduate students, and contractors. The EDRP provided examples showing increased coordination and integration of technical and science staff positions across different long-term goals (LTGs) and research programs thereby enhancing the impact of research activities. ORD has been proactive in developing core capacities in new molecular technologies (genomics, proteomics, and metabolomics) and systems biology and using these resources in cross-ORD projects. The Agency has been proactive in addressing gaps in research coverage by leveraging through the STAR Program and across agencies. Examples are provided below in relation to the LTGs. Finally, there is evidence of new improved administration and coordination of the ORD research programs at the senior levels of management that will facilitate program formulation and delivery of the EDRP. The program, however, has had to delay or eliminate some program goals because of reductions in allocated resources.

Long-Term Goal 1 of the EDRP is focused on a more in-depth understanding of the "science underlying the effects, exposure, assessment, and management of endocrine disruptors" and, in the 2004 program review, the BOSC outlined several challenges and recommendations. The breadth of the science associated with understanding the complexity of the endocrine control of growth, development, and reproduction along with the knowledge that multiple chemicals in the environment modulate these processes illustrate the enormity of this LTG. **To the program's credit, the EDRP continues to provide scientific results that will reduce the uncertainty regarding EDCs and facilitate science-based environmental decision-making.**

The types of questions being addressed by the EDRP merit specific mention. This includes studies of: (1) low-dose effects, developing appropriate animal models; (2) evaluation of mixtures of EDCs; (3) species extrapolation; (4) toxicogenomics in risk assessment; and (5) biomarkers and screening tools. These topics represent many of the critical uncertainties within the discipline and progress achieved by the EDRP in many of these has been rapid. This has been due, in part, to development of fruitful collaborations and interactions between various EPA laboratories and with other investigators. In particular, ORD scientists greatly expanded their network of scientific interactions to address issues on EDCs and this included other EPA laboratories (e.g., National Health and Environmental Effects Research Laboratory [NHEERL], Duluth; the National Exposure Effects Research Laboratory [NERL], Cincinnati and Athens; the National Center for Computational Toxicology [NCCT], Research Triangle Park; and the National Center for Environmental Research [NCER]), scientists from other EPA offices, academic laboratories, and other government agencies (e.g., U.S. Department of Agriculture [USDA], Food and Drug Administration [FDA], U.S. Geological Survey [USGS], and Department of Energy) with interests in EDCs and their adverse impacts.

One of the specific concerns highlighted in the 2004 BOSC program review report was that coverage of wildlife toxicology was limited relative to other areas that focused on human and aquatic species. **Addressing wildlife toxicology has continued to be a challenge for the program given the significant budgetary pressures that it is facing.** Recent efforts by the EDRP have included a February 2007 workshop across ORD programs and federal agencies in an effort to identify shared research activities and areas for increased collaborations. This has been aided by the progress in identifying the current state of the science regarding wildlife species, which is included in the draft document, Advancements in Endocrine Disruptors Research: Summary of US EPA Accomplishments 1996-2007, Chapter 4, Exposure and Effects in Wildlife.

On a related topic, the BOSC noted the complexities in extrapolating among the many species in the environment that may be affected by endocrine disruptors and the need for ORD to better characterize the range of vulnerability among species. **The Subcommittee notes that species extrapolation has been an area where the EDRP has been very active.** There has been research on the homology of the androgen and estrogen receptor and studies on the regulation of aromatase activity, steroidogenesis, and the thyroid axis through to the development of physiologically based pharmacokinetic models, each involving testing in multiple classes of vertebrates Understanding the conservation of molecular endocrine physiology across phyla is fundamental to determining if EDCs may affect species differently and is a critical component of the risk assessment process.

One of the recommendations of the 2004 program review was to further develop predictive tools for prioritizing specific EDCs and to evaluate the effectiveness of specific treatment technologies such as those related to water and wastewater treatment. In response, the EDRP has expanded research on developing predictive tools for determining the potential toxicity of chemicals by partnering with other Agency programs. There has been excellent progress made in response to this recommendation, and this has been bolstered by a strong partnership with ORD's Computational Toxicology Program. This has included work on the quantitative structure activity relationships (QSARs) for sorting chemicals based on mode of action. **The Subcommittee notes that EPA has been at the forefront of using genomics, proteomics, metabolomics, computational modeling, and whole animal endpoints to identify biomarkers of exposure to EDCs.** The EDRP has started to use these tools to prioritize treatment technologies for compounds of concern but progress in the area of risk management has been delayed, in part, because of the reductions in resources. In addition, the EDRP has taken the lead with respect to understanding the risks posed by concentrated animal feeding operations (CAFOs), which were identified as a major concern by the BOSC during the 2004 program review.

In 2004, the BOSC noted that the model and framework for EDC risk assessment are well established and recommended that efforts should now focus on the development of risk assessment paradigms of EDCs and application of the research findings. In response, the EDRP stated that current approaches for risk assessment on specific endpoints are appropriate for use in evaluating EDCs and that research by other scientists is routinely monitored. The EDRP is focusing its efforts on studying the impact of cumulative risks for groups of compounds with similar modes of actions and is doing innovative work on the disruption of the thyroid and androgen systems. This research is at the forefront of the field in evaluating the suitability of response additivity or dose additivity models when considering chemicals with both similar and dissimilar mechanisms of action. **As such, the Subcommittee finds that the EDRP is addressing the appropriate scientific questions to meet its goal**.

Long-Term Goal 2 is focused on determining the impact of EDCs on humans, wildlife, and the environment. Historically, this has been an area where the EDRP has been engaged in productive, high-quality research that is highly relevant to the mission of EPA. In 2004, the BOSC commented that EPA should continue to improve its interactions with other agencies that have a strong interest in EDCs to identify new sources of environmental and human exposure, including investigating the role of pharmaceuticals as sources of EDCs.

Many of the recommendations from the 2004 program review have been addressed, including partnering with other agencies with interests in EDCs. In particular, EPA has been active in two Intra-agency Working Groups (IWGs) focused on EDCs in the environment and pharmaceuticals in the environment. EPA has taken the lead in evaluating natural and synthetic hormones in CAFOs as well as a prominent role in furthering research in wastewater, biosolids, and drinking water applications. There have been collaborations with numerous EPA regional offices, EPA's Office of Water, states, and trade organizations in evaluating the downstream impacts and treatment technologies related to wastewater treatment plants. As such, the EDRP is

meeting its goals in addressing the appropriate scientific questions associated with this 2004 BOSC recommendation.

One of the most difficult and expensive challenges has been the epidemiologic studies that have shown some progress and have received funding from other agencies. **Epidemiology is clearly not an area of traditional strength for EPA and, due to limited resources, this is an area that should continue to be partnered with other agencies** such as the Centers for Disease Control and Prevention (CDC), National Institute of Environmental Health Sciences (NIEHS), and other National Institutes of Health (NIH) institutes. There have been some successes in this regard through the STAR Program.

A further recommendation from the 2004 program review under LTG 2 was that EPA should take a leadership role in the application of "omics" technologies to address many of the science questions critical for evaluating environmental and human effects of EDCs. **As mentioned under LTG 1 above, "omics" technologies are an area of strength within EPA** and this has been evident in the Agency studies investigating the effects of estrogenic compounds in fish and the characterization of the actions of fungicides on the male reproductive tract in rodents. There are ongoing plans for using the genomic technologies in assessing the effects of dibutyl phthalate in health risk assessment. Long-range planning should incorporate a systems biology approach that addresses critical endpoints because this type of integrated approach can be highly predictive for evaluating different compounds.

The 2004 BOSC program review also recommended that EPA consider the integration of ecological and human health risk assessment. **Owing to budget constraints, there has been modest progress in addressing the integration of ecological and human health assessment,** although a number of past and ongoing studies may provide suitable test cases to evaluate the utility of combined ecological and human health assessments.

Long-Term Goal 3 is focused on the screening and testing program that has made significant progress since the program review. Various *in vitro* and *in vivo* assays have or are undergoing evaluation. In addition to recommendations for strengthening "omics" technologies, the funded Computational Toxicology Program should be important resources for data handling and analysis of the "future" screening and testing programs.

In 2004, the BOSC noted that the transfer of protocols to contract laboratories had been problematic and recommended that there be a mechanism in place to ensure the timely transfer of protocols to EPA's Office of Prevention, Pesticides, and Toxic Substances (OPPTS). In response, the EDRP commented that significant progress has been made in completing the research needed to develop and standardize assays for the Agency's EDSP. In 2004, the BOSC noted the progress that had been made in genomics and QSAR methods and recommended that ORD train or hire experts in bioinformatics to work with the life sciences experts already on board. In response, the EDRP provided evidence that significant progress has been made in this area and described the establishment of genomics and metabolomics cores, cooperative efforts, new hires, and establishment of new centers in these areas. **As such, the EDRP has demonstrated a speedy response and development of resources for producing high-quality science in response to these 2004 recommendations.**

B. Charge Question #2

To what extent does the updated draft MYP provide a coherent framework and rationale for addressing priority research needs?

Overall, the new draft MYP is excellent. The goals are streamlined, and the outcome-oriented language makes them much better to assess progress. Now that the program has matured, the updated draft MYP has set the stage for future research. The MYP highlights the focus of EPA's contributions, and it emphasizes the contributions that EPA can make based on its strengths. Although this Subcommittee did not provide an extensive review of the MYP details as part of its charge, it can comment on the MYP's framework for providing a roadmap for the future.

The Subcommittee finds that the updated draft MYP is logical, and information is well supported in providing a coherent framework and rationale for addressing priority research needs of the EDRP. The updated draft MYP sets the stage for the work of the EDRP by acknowledging historical EDC work that has been done by individual scientists and EPA laboratories for several decades, by describing the formal initiation of the program with two workshops in 1995, and by discussing modifications and revisions to the program over the years. In addition, the updated draft MYP clearly defines the purpose of the EDRP, the Agency's adopted definition of endocrine disruptors, and the focus of the EDRP as stated in terms of its three LTGs.

The updated draft MYP provides an informative background on how the EDRP fits into the Agency's priorities, and the relationship of the EDRP to other organizations such as the U.S. Department of the Interior (DOI), National Oceanic and Atmospheric Administration (NOAA), FDA, and DOE; industry; and the international community. Finally, the updated draft MYP highlights the progress to date and changes from the previous version in terms of each of the three LTGs. The considerable progress already made by the EDRP on reaching milestones in its MYP is evidence that the plan is serving its intended purpose and that its goals are on target.

C. Charge Question #3

Are there performance metrics the EDRP should be using in addition to the current indicators (e.g., quality and impact of ORD publications, timeliness of completing goals) for regularly assessing research progress?

Performance metrics for programs are to be developed and applied with great caution. Assessing the performance of a new scientific program is of particular concern, as many traditional metrics were developed for assessing sustained, long-term progress and do not apply. Given that the success of the EDRP has been notably hampered by budgetary constraints in recent years, **the Subcommittee suggests that the metrics be considered carefully and in the context of**

budget, full-time equivalents (FTEs), and the amount of time a particular activity has been underway.

The performance metrics used to quantify the impact of EPA's EDRP were interesting and, using multiple criteria, clearly demonstrated the high quality of the research relative to other publications in the field. Performance metrics on a relatively new program are difficult to gauge. For example, a metric equal to the number of citations for a publication is useful for a long-term program but would be lower and thus disadvantage a new program. Sufficient time must elapse for other investigators to appreciate and cite the work.

Additional metrics that should be developed are those related to the level of collaboration and/or interaction between members of the EDRP with other agencies, academia, industry, and in the international community.

Additional metrics that assess how the research outcomes are being used in decision-making should be developed. The Subcommittee recognizes that such metrics are more difficult to develop relative to the ones suggested above, but it is an overarching goal to connect the science developed in ORD with decision-making, regulation, and management. The workshops with scientists, Agency staff, stakeholders, and decision-makers that have taken place (e.g., the recent CAFO-EDCs workshop in August 2007) are a great step towards improving communication and helping to inform decision-makers. **Metrics that assess these kinds of communication exchanges, and whether they are involving the appropriate people, should be considered.**

The Subcommittee recommends that other performance metrics that will provide an impact of the science and the investigators be considered, and these include the following:

- Number of publications in high impact journals (as a percentage of the total).
- Distribution of papers published in journals with low to high citation indices.
- Number of invitations to program scientists to present their results at national and international meetings (not organized or sponsored by EPA).
- Other scientific recognition (e.g., awards) to scientists participating in the EDRP.
- Number and percentage of intra- and inter-agency and laboratory collaborative publications.
- Number of EPA EDRP scientists serving on journal editorial boards.
- Number of EPA EDRP scientists serving on scientific advisory councils or boards.

It is acknowledged that the Bibliometric Analysis that was provided to the Subcommittee was an aggregate of performance for both EPA researchers and extramural colleagues. This is important

information, and an aggregate analysis as well as a separate reporting of these measures for EPA scientists should be considered.

D. Charge Question #4

Since the 2004 BOSC review, the EDRP has made significant advances in developing assays for use in the Agency's screening and testing program. As a result, that effort will decline in the future with a greater research emphasis on how to interpret data for risk assessment and further characterization of the impact of EDCs in the environment. In addition, since the 2004 review there have been significant decreases in the resources allocated to the EDRP. What advice can the BOSC provide regarding the planned narrower focus and directions of the EDRP given its evolution and budget impacts? For example, are there other higher priority or emerging research areas that ORD should consider, in lieu of what is planned?

The Subcommittee is supportive of the direction and priorities that have been identified already by the EDRP through the MYP, and its anticipated long-term outcomes. **The Subcommittee encourages the program to continue its ongoing evaluation and planning activities. Obvious research gaps or needs that currently are not acknowledged by the EDRP were not identified.** The Subcommittee recognizes that research on EDCs has and will continue to be a priority for EPA in the foreseeable future, and it is clear that the main efforts of the EDRP will need to be on LTGs 1 and 2.

Since the 2004 program review, the EDRP has had to make decisions about its projects and priorities, as it already has experienced funding reductions. The EDRP has emphasized leveraging by engaging in strategic partnerships with other agencies and researchers and this approach should be continued.

The Subcommittee recognizes that EPA has achieved significant leadership in EDC research, and encourages the ERDP to take on an even more visible leadership role in risk management by:

- Compiling and synthesizing what is known about occurrence and exposure.
- Advising the end users in the water, wastewater, and water-reuse industries on priorities for integrated water systems, and connecting them to a synthesis of the current EDC literature.
- Strengthening relationships with professional organizations, private research foundations, academia, and industry to identify research funding and prioritizing research needs in addressing effective risk management of EDCs.

- Strengthening the program's relationships with relevant national and international agencies.

- Building and strengthening opportunities for education and outreach with stakeholders as well as the general public.

In addition, the **Subcommittee recommends that EPA and other regulatory agencies (national and international) consider more harmonization regarding the results of EDC scientific studies and their applications for risk assessment**. Long-range planning may want to incorporate a systems biology approach that addresses critical endpoints because this type of integrated assay can be highly predictive for evaluating different compounds. Pharmaceutical companies increasingly rely on the predictive capabilities of systems biology.

Finally, **should extramural funds become available to the EDRP, the program should use them for cooperative agreements** to encourage collaborations of EPA scientists with those in the academic research community and to strategically complement their expertise.

E. Charge Question #5

Please rate the progress made by the EDRP in moving the program forward in response to the BOSC review of 2004 by assigning a qualitative score, i.e., exceptional, exceeds expectations, meets expectations, or not satisfactory. The score should be in the form of one of the adjectives defined in Appendix 2. This uniform rating system is intended to promote consistency among BOSC reviews. The adjectives should be used as part of a narrative summary of the review, so that the context of the rating and the rationale for selecting a particular rating will be transparent. For mid-cycle reviews, the rating should be based on the quality, speed, and success of the program's actions in addressing previous BOSC recommendations. The adjectives to describe progress are found in Appendix B. Because this is a mid-cycle review, the Subcommittee is addressing progress rather than reporting on an extensive technical evaluation of the program's goals.

The rating of the EDRP by this Subcommittee is based on the quality, speed, and success of the program's actions in addressing previous BOSC recommendations. A brief justification and rating for these three criteria are presented below.

In terms of quality, the EDRP has consistently demonstrated work products that are rated as exceeding expectations or exceptional. This program has established itself as a leader in several areas of EDC research, with limited resources. The bibliometric analysis shows that the percentage of EDRP papers published in journals with a high JCR Impact Factor is 4.1 times higher than the expected percentage and the percentage of EDRP papers published in journals with a high JCR Immediacy Index is 4.4 times higher than the expected percentage. In addition, the EDRP has developed an excellent new MYP. Based on quality, the EDRP is rated "exceptional."

With regard to speed, the EDRP meets its goals or provides reasonable justification for delaying the specific goals based on limited available budgetary resources. Some goals have been successfully accomplished by innovative leveraging of expertise across the Agency and with other federal and academic scientists, whereas other goals have been justifiably delayed. As such, with respect to this criterion, the EDRP "exceeds expectations."

In terms of success, the EDRP is rated as "meets expectations." The program is meeting most of its goals. The EDRP has been quick to respond and adapt its focus and research questions to the rapidly changing research landscape of EDCs. The budget for this program has declined 20 percent since its last program review. If this trend continues, it is not feasible that the EDRP can meet all of its previously stated goals.

Considering the three criteria as discussed above, the overall rating of the progress in moving the EDRP forward is rated by this Subcommittee as "exceeds expectations."

IV. APPENDICES

Appendix A: Endocrine Disrupting Chemicals Mid-Cycle Review Subcommittee

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Appendix B:
Rating Tool Adjectives Used to Describe Progress

- **Exceptional**: indicates that the program is meeting all and exceeding some of its goals, both in the quality of the science being produced and the speed at which research results, tools, and methods are being produced. An exceptional rating also indicates that the program is addressing the right questions to achieve its goals. The review should be specific as to which aspects of the program's performance have been exceptional.

- **Exceeds Expectations**: indicates that the program is meeting all of its goals. It addresses the appropriate scientific questions to meet its goals, and the science is competent or better. It exceeds expectations for either the high quality of the science or for the speed at which work products are being produced and milestones met.

- **Meets Expectations**: indicates that the program is meeting most of its goals. Programs that meet expectations live up to them in terms of addressing the appropriate scientific questions to meet their goals, and work products are being produced and milestones are being reached in a timely manner. The quality of the science being done is competent or better.

- **Not Satisfactory**: indicates that the program is failing to meet a substantial fraction of its goals, or if meeting them, that the achievement of milestones is significantly delayed, or that the questions being addressed are inappropriate or insufficient to meet the intended purpose. Questionable science also is a reason for rating a program as unsatisfactory for a particular long-term goal. The review should be specific as to which aspects of a program's performance have been inadequate.

Appendix C: List of Acronyms

BOSC	Board of Scientific Counselors
CAFO	Concentrated Animal Feeding Operation
CDC	Centers for Disease Control and Prevention
DOE	U.S. Department of Energy
DOI	U.S. Department of the Interior
EDC	Endocrine Disrupting Chemical
EDRP	Endocrine Disruptors Research Program
EDSP	Endocrine Disruptor Screening Program
EPA	U.S. Environmental Protection Agency
FACA	Federal Advisory Committee Act
FDA	U.S. Food and Drug Administration
FTEs	Full-Time Equivalents
IWG	Intra-agency Working Group
LTG	Long-Term Goal
MYP	Multi-Year Plan
NCCT	National Center for Computational Toxicology
NCER	National Center for Environmental Research
NERL	National Exposure Research Laboratory
NHEERL	National Health and Environmental Effects Research Laboratory
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NOAA	National Oceanic and Atmospheric Administration
OPPTS	Office of Prevention, Pesticides, and Toxic Substances
ORD	Office of Research and Development
USDA	U.S. Department of Agriculture
USGS	U.S. Geological Survey
QSAR	Quantitative Structure Activity Relationship