

## Workshop 6.8

# Advancing the testing and assessment of chemical substances for endocrine disruption: OECD activities\*

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*Abstract:* This paper describes the establishment of a number of expert groups in the Organization for Economic Cooperation and Development (OECD) to manage the work related to the development and validation of test methods to identify and characterize the human health and aquatic environmental hazards of endocrine-disrupting chemicals. In addition, the concept of testing and assessment, using the most adequate testing tools without being prescriptive, is explained, and a coordinated approach for international work sharing under the OECD umbrella is described.

## INTRODUCTION

The most important aspect of the Organization for Economic Cooperation and Development (OECD) work of the Environment, Health, and Safety Division focuses on the regulatory management of chemicals, taking into account the possible effects of chemicals on human health and the environment. In the context of the Chemicals Program, the work covers chemicals, and includes, e.g., industrial chemicals and pesticides. In 1996, the OECD launched a Special Activity on Endocrine Disruptor Testing and Assessment with the following objectives of:

- providing information and coordinating activities;
- developing new and updated Test Guidelines to detect endocrine disruptors; and
- harmonizing hazard and risk characterization approaches.

This activity was initiated at the request of the Member countries and the Business and Industry Advisory Committee (BIAC) to the OECD to promote that testing and assessment approaches for endocrine disruptors would not substantially differ among countries. In order to manage the work of the Special Activity, the Task Force on Endocrine Disruptors Testing and Assessment (EDTA) was established in the same year.

## DEVELOPMENT AND VALIDATION OF TEST METHODS

In the first years of the Special Activity, the focus was largely on developing new and updating existing test methods. The development of selected tests as OECD Test Guidelines involved formal validation of these tests. To that end, validation management groups (VMGs) were established to validate mammalian tests (VMG-mammalian) and ecotoxicity tests (VMG-eco), respectively. In June 2002, the

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\*Report from a SCOPE/IUPAC project: Implication of Endocrine Active Substances for Human and Wildlife (J. Miyamoto and J. Burger, editors). Other reports are published in this issue, *Pure Appl. Chem.* **75**, 1617–2615 (2003).

EDTA agreed that a third VMG was needed to validate *in vitro* and other nonanimal tests (VMG-*in vitro*). Current test method development and validation activities include:

- uterotrophic assay [to detect mammalian (anti)estrogen-mimicking substances];
- Hershberger assay [to detect mammalian (anti)androgen-mimicking substances];
- enhancement of Test Guideline 407 [to detect (anti)estrogen, (anti)androgen, and thyroid hormone-related effects in mammals];
- fish screening and full life-cycle tests and reproduction test(s) in birds (to screen and test antiestrogens and antiandrogen effects);
- amphibian metamorphosis test (for thyroid hormone function disruption); and
- invertebrate tests.

### CONCEPTUAL FRAMEWORK FOR TESTING AND ASSESSMENT APPROACHES

To provide a framework for the testing and assessment of potential endocrine disruptors in which the various newly developed tests would fit, a conceptual framework was developed. The conceptual framework is intended to apply to both new and existing substances as well as for different chemical sectors such as pharmaceuticals, industrial chemicals, and pesticides. It was developed taking into account:

- The views of Member countries as expressed through answers to a questionnaire and the OECD's Appraisal of Test Methods for Sex Hormone and Disrupting Chemicals (OECD Monograph No. 21).
- Proposed testing schemes such as those developed at relevant workshops, notably the European Workshop on the Impact of Endocrine Disruptors on Human Health and Wildlife (the Weybridge Workshop), and the Joint Society of Environmental Toxicologists and Chemists (SETAC) and OECD/EC Expert Workshop on Endocrine Modulators and Wildlife: Assessment and Testing (the EMWAT Workshop).
- The work of national activities such as the U.S. Environmental Protection Agency's (USEPA's) Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC) and research activities in Japan.
- Industry initiatives such as those being undertaken by the European Chemical Industry Council (CEFIC).

The conceptual framework has been reconsidered and substantially revised by the EDTA in its June 2002 meeting in Tokyo. There it was confirmed that the conceptual framework is not a testing scheme, but rather a toolbox to place the various tests that can contribute information for the detection of the hazards of endocrine disruption. The toolbox is organized into several compartments or levels, each corresponding to a different level of biological complexity (for both toxicological and ecotoxicological areas). Even though the toolbox may be full of testing tools, this does not imply that they all will be needed for assessment purposes.

### SHARING THE WORK OF TESTING AND ASSESSMENT

As this ongoing cooperative work on test method development is starting to bear fruit and the tools for testing and assessment of possible endocrine disruptors are taking shape, the next step in the process was to start using these tools. Considering (i) the vast amount of chemicals currently in use that need to be considered, (ii) the time pressure to identify and assess endocrine-disrupting chemicals as expeditiously as possible, (iii) the number of studies necessary for screening and, as appropriate, full hazard assessment, and (iv) the lack of resources needed for this work, it was considered appropriate to find ways to share (at least some of) the work internationally. In June 2001, Member countries agreed to

share the actual testing of existing substances for possible endocrine-disrupting activities and to find ways to share assessments of tested chemicals. Member countries further agreed that the work-sharing activity should start as a small activity that could gradually increase if proven successful. First priority would include grouping chemicals of interest, sharing information and test results of high-throughput screens, and exchanging information on ongoing animal tests. Sharing assessment reports of specific substances was also considered extremely useful. This work has now begun and will be expanded in coming years.