BILLING CODE 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-OPPT-2014-0766; FRL-9919-43]

Draft Test Guidelines; Endocrine Disruptor Screening Program Test Guidelines (Series 890); Three Tier 2 Non-Mammalian Tests; Notice of Availability and Request for Comment

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA is announcing the availability of three draft test guidelines for public review and comment that are being added to its 890 Series, entitled "Endocrine Disruptor Screening Program Test Guidelines." The draft guidelines relate to the following three non-mammalian species tests identified under Tier 2 of the Endocrine Disruptor Screening Program (EDSP): Japanese quail 2-generation reproduction test; Medaka extended 1-generation reproduction test; and Larval amphibian growth and development assay. These draft test guidelines are part of a series of test guidelines established by the Office of Chemical Safety and Pollution Prevention (OCSPP) for use in testing pesticides and chemical substances. The test guidelines serve as a compendium of accepted scientific methodologies and protocols that are intended to provide data to inform regulatory decisions. The test guidelines provide guidance for conducting the test, and are also used by EPA, the public, and companies that submit data to EPA.

DATES: Comments must be received on or before [*insert 60 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit your comments, identified by docket identification (ID) number EPA-HQ-OPPT-2014-0766, by one of the following methods:

• *Federal eRulemaking Portal*: *http://www.regulations.gov*. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.

• *Mail*: Document Control Office (7407M), Office of Pollution Prevention and Toxics (OPPT), U.S. Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

• *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.html*.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets*.

FOR FURTHER INFORMATION CONTACT: Sharlene Matten, telephone number: (202) 564-0130, email address: *matten.sharlene@epa.gov;* or Steven Knott, telephone number: (202) 564-0103, email address: *knott.steven@epa.gov*. Mailing address: Office of Science Coordination and Policy (7201M), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

SUPPLEMENTARY INFORMATION:

I. Introduction

EPA is announcing the availability of three draft test guidelines for public review and comment that are being added to its 890 Series, entitled "Endocrine Disruptor Screening Program Test Guidelines." The draft guidelines relate to the following three non-mammalian species tests identified under Tier 2 of the EDSP: Japanese quail 2-

generation reproduction test; Medaka extended 1-generation reproduction test; and Larval amphibian growth and development assay.

These draft test guidelines are part of a series of test guidelines established by OCSPP for use in testing pesticides and chemical substances to develop data for submission to the Agency under the Federal Food, Drug and Cosmetic (FFDCA) section 408 (21 U.S.C. 346a), the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et seq.*), and the Toxic Substances Control Act (TSCA) (15 U.S.C. 2601 *et seq.*). The test guidelines serve as a compendium of accepted scientific methodologies and protocols that are intended to provide data to inform regulatory decisions under TSCA, FIFRA, and/or FFDCA.

The test guidelines provide guidance for conducting the test, and are also used by EPA, the public, and companies that are subject to data submission requirements under TSCA, FIFRA, and/or FFDCA. As guidance documents, the test guidelines are not binding on either EPA or any outside parties, and EPA may depart from the test guidelines where circumstances warrant and without prior notice. At places in this guidance, the Agency uses the word "should." In this guidance, use of "should" with regard to an action means that the action is recommended rather than mandatory. The procedures contained in the test guidelines are recommended for generating the data that are the subject of the test guideline, but EPA recognizes that departures may be appropriate in specific situations. You may propose alternatives to the recommendations described in the test guidelines, and the Agency will assess them for appropriateness on a case-by-case basis.

II. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general. Although this action may be of particular interest to those persons who are or may be required to conduct testing of pesticides and chemical substances for submission to EPA under TSCA, FIFRA, and/or FFDCA, the Agency has not attempted to describe all the specific entities that may be affected by this action.

B. What Should I Consider as I Prepare My Comments for EPA?

1. *Submitting CBI*. Do not submit this information to EPA through regulations.gov or email. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD-ROM that you mail to EPA, mark the outside of the disk or CD-ROM as CBI and then identify electronically within the disk or CD-ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments*. When preparing and submitting your comments, see the commenting tips at *http://www.epa.gov/dockets/comments.html*.

III. Overview

A. What is the EDSP?

The EDSP is established under FFDCA section 408(p), which requires EPA to develop a chemical substance screening program using appropriate validated test systems and other scientifically relevant information to determine whether certain chemical

substances may have hormonal effects. The EDSP consists of a two-tiered approach to screen chemical substances for potential endocrine disrupting effects. The purpose of Tier 1 screening is to identify chemical substances that have the potential to interact with the estrogen, androgen, or thyroid hormone systems using a battery of assays. Chemical substances that have the potential to interact with the estrogen, androgen or thyroid systems may proceed to Tier 2 testing, which is designed to identify any adverse endocrine-related effects caused by the chemical substance, and to establish a quantitative relationship between the dose and that endocrine effect. Additional information about the EDSP is available at *http://www.epa.gov/endo*.

1. *Tests considered for EDSP Tier 2.* In the December 1998 EDSP Policy Statement (Ref. 1), the Agency explained that the purpose of the testing stage (Tier 2) is to characterize the likelihood, nature, and dose-response relationship of any estrogen-, androgen-, and thyroid-related effects caused by a chemical substance in humans or wildlife. At that time, EPA identified the following non-mammalian tests under Tier 2 of EDSP: Amphibian reproduction and developmental toxicity, avian reproduction, fish reproduction, and invertebrate reproduction.

EPA followed the general validation principles of the Organization for Economic Co-Operation and Development (OECD) and the Intergovernmental Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) in the development of the four non-mammalian Tier 2 tests. In June 2013, the FIFRA Scientific Advisory Panel (SAP), a Federal advisory committee chartered under the Federal Advisory Committee Act (5 U.S.C. Appendix), reviewed draft protocols and supporting data for the four non-mammalian Tier 2 tests (Ref. 2): Japanese quail 2-generation

toxicity test; Medaka extended 1-generation reproduction test; Larval amphibian growth and development assay; and mysid 2-generation toxicity test.

2. *Status of the mysid 2-generation toxicity test.* Although the mysid 2-generation toxicity test was generally supported by the FIFRA SAP, the data were not considered fully reliable across all endpoints and the results were not repeatable across laboratories without recommended improvements (Ref. 2). The FIFRA SAP and public commenters also stated that endpoints in the mysid 2-generation toxicity test are also provided to a large extent by the current mysid chronic life cycle test (Ref. 3), a test used effectively to assess the risk of chemical substances that may disrupt invertebrate growth, development, and reproduction, such as, insect growth regulators that disrupt development mediated by invertebrate hormones (Ref. 2). While concerns were expressed for certain aspects of the mysid 2-generation toxicity test, there were advancements in other features of the assay, particularly regarding culturing conditions and control performance.

Based on all of these factors, the Agency intends to consider and potentially incorporate, as appropriate, test design features from the mysid 2-generation toxicity test when updating and finalizing the existing draft mysid chronic life cycle test guideline (Ref. 4) assessing development, growth, reproductive, and toxicity endpoints. This may include the option of extending the mysid chronic life cycle test to a second generation. Expansion of the mysid chronic life cycle test was one of the Agency's options discussed in the December 1998 EDSP Policy Statement (Ref. 1). The existing OCSPP Test Guideline 850.1350 is intended to meet current and future testing requirements for data submitted to EPA under FFDCA, FIFRA, and TSCA (Ref. 4).

B. How Were The Draft Test Guidelines Developed?

The FIFRA SAP supported the scientific rationale and purpose, representative species chosen, biological and toxicological relevance of the major endpoints selected and measured, and the validation process used by EPA for all four Tier 2 non-mammalian tests (Ref. 2). Based on the FIFRA SAP's recommendations and public comments received, the EPA revised the test protocols (Ref. 3) and developed draft test guidelines for the following three tests: Japanese quail 2-generation toxicity test, Medaka extended 1-generation reproduction test, and Larval amphibian growth and development assay.

• The Japanese quail 2-generation reproduction test features a number of core apical endpoints related to survival, growth, reproduction and, potentially, behavior, as well as more pathway-specific endpoints (e.g., histopathology). See draft OCSPP Test Guideline 890.2100, entitled "Endocrine Disruptor Screening Program Test Guidelines; Avian Two-generation Toxicity Test in the Japanese Quail."

• The Medaka extended 1-generation reproduction test, developed and evaluated primarily by scientists from the United States and Japan, starts with F0 adults, proceeds through the entire F1 generation, and provides an option for an entire life cycle exposure of the F2 generation. The test, which features both pathway-specific (e.g., histopathology) and apical (e.g., growth, reproduction) endpoints, has been successfully evaluated using several chemical substances expected to have different effects on the hypothalamic-pituitary-gonadal (HPG) axis. See draft OCSPP Test Guideline 890.2200, entitled "Endocrine Disruptor Screening Program Test Guidelines; Medaka Extended One Generation Reproduction Test (MEOGRT)."

• The Larval amphibian growth and development assay is designed to assess possible risks of both HPG- and hypothalamic-pituitary-thyroid (HPT)-active toxicants.

The assay, which was also developed through a joint effort between the United States and Japan, is initiated with Nieuwkoop-Faber (NF) stage 8 embryos and proceeds through NF stage 62 (complete metamorphosis). The amphibian test considers a variety of both apical and more pathway-specific endpoints. See draft OCSPP Test Guideline 890.2300, entitled "Endocrine Disruptor Screening Program Test Guidelines; Larval Amphibian Growth and Development Assay (LAGDA)."

IV. References

The following is a listing of the documents that are specifically referenced in this document. The docket includes these documents and other information considered by EPA, including documents that are referenced within the documents that are in the docket, even if the referenced document is not physically located in the docket. For assistance in locating these other documents, please consult the persons listed under **FOR FURTHER INFORMATION CONTACT**.

1. EPA. Endocrine Disruptor Screening Program; Proposed Statement of Policy; Notice**. Federal Register** (63 FR 71542, December 28, 1998) (FRL-6052-9).

2. FIFRA SAP. SAP Minutes No. 2013-04. A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: Proposed Endocrine Disruptor Screening Program (EDSP) Tier 2 Ecotoxicity Tests, June 25-28, 2013. 2013. Docket ID No. EPA-HQ-OPP-2013-0182-0084.

3. EPA. Summary of EPA's Responses to Recommendations of the June 25-28, 2013 FIFRA SAP Regarding Proposed EDSP Tier 2 Non-Mammalian Tests. 2014.

4. EPA. OCSPP Harmonized Ecological Effects Test Guideline 850.1350 (Public Draft): Mysid Chronic Toxicity Test, April 1996. EPA 712–C–96–166. 1996. Docket ID No. EPA-HQ-OPPT-2009-0154.

Authority: 7 U.S.C. 136 *et seq.*; 15 U.S.C. 2601 *et seq.*; 21 U.S.C. 346a.

Dated: December 23, 2014.

Louise P. Wise,

Acting Assistant Administrator, Office of Chemical Safety and Pollution Prevention.

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