



## U.S. Environmental Protection Agency

# Endocrine Disruptor Screening Program

[Recent Additions](#) | [Contact Us](#) | [Print Version](#) Search:  [GO](#)

[EPA Home](#) > [Office of Prevention, Pesticides, and Toxic Substances](#) > [Office of Science Coordination and Policy](#) > [Endocrine Disruptors](#) > [EDSP Overview](#) > EDSP Primer

[EDSP Overview](#)

[Assay Development and Validation](#)

[Priority Setting Activities](#)

[Regulatory Aspect](#)

[Program Documents](#)

[Stakeholder Input](#)

[Related Links](#)

## Endocrine Primer

Click on a link below to access an overview of the endocrine system, information on endocrine disruptors, and general information about the Endocrine Disruptor Screening Program (EDSP).

[Endocrine System Overview](#)

[Endocrine Disruptors](#)

[Endocrine Disruptor Screening Program](#)

[Endocrine Disruptor Screening Program History](#)



## Endocrine System Overview

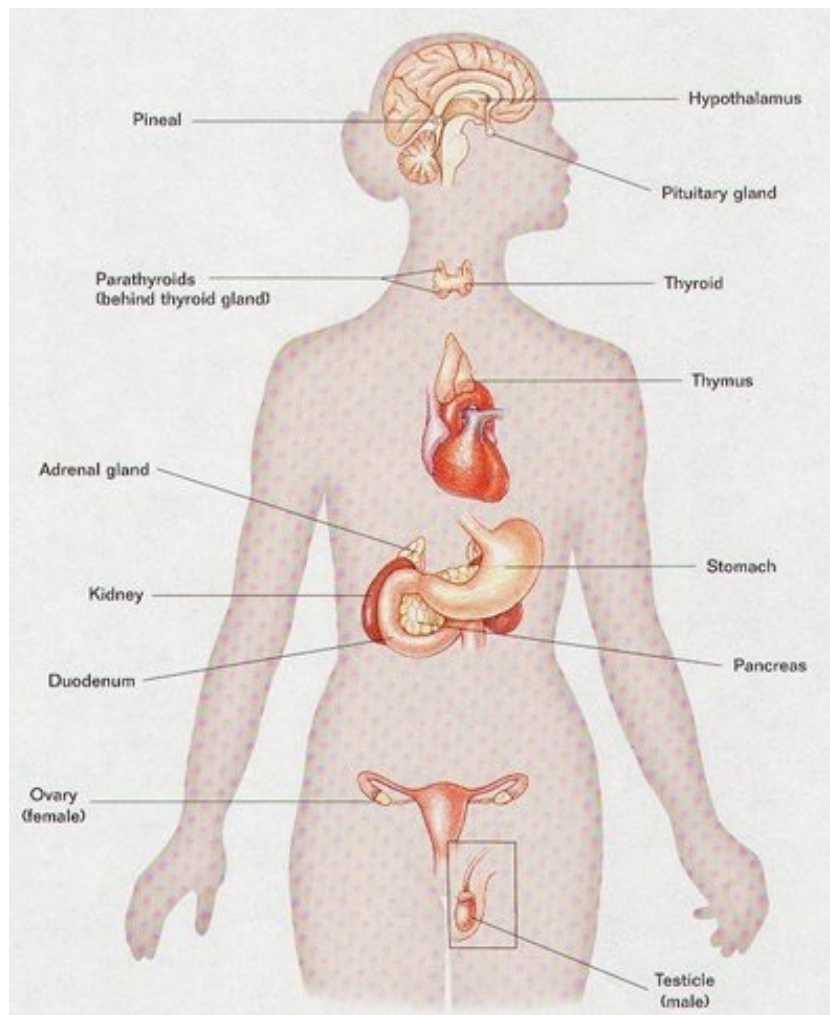
The endocrine system, also referred to as the hormone system, is found in all mammals, birds, and fish. It is made up of:

- Glands located throughout the body.
- Hormones (i.e., chemical messengers) that are made by the glands and released into the bloodstream or the fluid surrounding cells.
- Receptors in various organs and tissues that recognize and respond to the hormones.

Hormones are released by glands and travel throughout the body searching for cells that contain matching receptors-proteins within the target cell or located on the surface of the target cell. The hormone binds with the receptor, much like a key would fit into a lock to unlock a door. The hormones, or keys, need to find compatible receptors, or locks, to work properly. Although hormones reach all parts of the body, only target cells with compatible receptors are equipped to respond. Once a receptor and a hormone have bonded, the receptor carries out the hormone's instructions by either altering the cell's existing proteins or turning on genes that will build a new protein. Both of these actions create reactions throughout the body. Researchers have identified more than 50 hormones in humans and other vertebrates.

The endocrine system regulates all biological processes from the conception of an organism through adulthood and into old age regulating many functions of a body, including metabolism, blood sugar levels, growth and function of the reproductive system, and the development of the brain and nervous system. The female ovaries, male testes, and pituitary, thyroid, and adrenal

glands are all endocrine glands.



The EPA's *Endocrine Disruptor Screening Program* focuses on the estrogen, androgen, and thyroid hormones. Estrogens, produced primarily by the ovaries and in small amounts by the adrenal glands, are the group of hormones responsible for female sexual development. Androgens are substances responsible for male sex characteristics. Testosterone, the sex hormone produced by the testicles, is an androgen. The thyroid gland secretes two main hormones, thyroxine and triiodothyronine, into the bloodstream that stimulate all the cells in the body and control many biological processes such as growth, reproduction, development, and metabolism.

**Endocrine glands are located throughout the human body:**

**Hypothalamus** - The hypothalamus links our endocrine and nervous systems together. The hypothalamus drives the endocrine system.

From *Biology: Principles and Explorations*, Teaching Transparencies. Copyright 1996 by Holt, Rinehart and Winston. All rights reserved. Reprinted by permission of the publisher.

**Pituitary gland** - The pituitary gland receives signals from the hypothalamus. This gland has two lobes, the posterior and anterior lobes. The posterior lobe secretes hormones that are made by the hypothalamus. The anterior lobe produces its own hormones, several of which act on other endocrine glands.

**Thyroid gland** - The thyroid gland is critical to the healthy development and maturation of vertebrates and regulates metabolism.

**Adrenal glands** - The adrenal gland is made up of two glands: the cortex and medulla. These glands produce hormones in response to stress and regulate blood pressure, glucose metabolism, and the body's salt and water balance.

**Pancreas** - The pancreas is responsible for producing glucagon and insulin. Both hormones help regulate the concentration of glucose (sugar) in the blood.

**Gonads** - The male reproductive gonads, or testes, and female reproductive gonads, or ovaries, produce steroids that affect growth and development and also regulate reproductive cycles and behaviors. The major categories of gonadal steroids are androgens, estrogens, and progestins, all of which are found in both males and females but at different levels. You can find additional information about the endocrine system on the Internet by opening a search engine and searching

on "endocrine", or try the Tulane University website at <http://e.hormone.tulane.edu/> EXIT Disclaimer

[Back to Top](#)

## Endocrine Disruptors

Disrupting the endocrine system can occur in various ways. Some chemicals can mimic a natural hormone, fooling the body into over-responding to the stimulus (e.g., a growth hormone that results in increased muscle mass) or responding at inappropriate times (e.g., producing insulin when it is not needed). Other endocrine disrupting chemicals can block the effects of a hormone from certain receptors. Still others can directly stimulate or inhibit the endocrine system, causing overproduction or underproduction of hormones. Certain drugs are used to intentionally cause some of these effects, such as birth control pills. In many situations involving environmental chemicals, an endocrine effect may not be desirable.

In recent years, some scientists have proposed that chemicals might inadvertently be disrupting the endocrine system of humans and wildlife. A variety of chemicals have been found to disrupt the endocrine systems of animals in laboratory studies, and compelling evidence shows that endocrine systems of certain fish and wildlife have been effected by chemical contaminants, resulting in developmental and reproductive problems. However, the relationship of human diseases of the endocrine system and exposure to environmental contaminants is poorly understood and scientifically controversial.

[Back to Top](#)

## The Endocrine Disruption Screening Program

The science related to measuring and demonstrating endocrine disruption is in its' infancy, so validated methods of testing that indicate specific effects of an endocrine disruptor are still being developed. The Endocrine Disruption Screening Program (EDSP) is mandated to use validated methods for the screening and testing chemicals to identify potential endocrine disruptors, determine adverse effects, dose-response, assess risk and ultimately manage risk under current laws. These methods or assays once developed and validated should allow EPA to identify and characterize the endocrine activity (specifically, estrogen, androgen and thyroid) of pesticides, commercial chemicals, and environmental contaminants. While EPA has some data on endocrine-disrupting pesticides, currently insufficient scientific data are available on most of the estimated 87,000 chemicals produced today to allow for an evaluation of of endocrine associated risks.

To address this issue, EPA is developing a two-tiered screening and testing process. In Tier 1, EPA hopes to identify chemicals that have the potential to interact with the endocrine system. In Tier 2, EPA will determine the specific effect caused by each endocrine disruptor and establish the dose at which the effect occurs. This approach will enable EPA to gather the information needed to identify endocrine disruptors and take appropriate regulatory action, as mandated by Congress. In 2001, EPA chartered the Endocrine Disruptor Methods Validation Subcommittee (EDMVS) under Federal Advisory Committee Act (FACA) and National Advisory Council for Environmental Policy and Technology (NACEPT). EDMVS provides people and organizations the opportunity to express their concerns and work to ensure that scientifically-sound validation processes are developed for animal- and non-animal-based screens and tests. EDMVS' mission is to critically examine every step of the validation process, provide advice to EPA, and suggest or consider new assays, or chemical tests. See the [Assay Status Table](#) for the current status of the Tier 1 and Tier 2 assays.

### Validated Methods Development

EPA's Endocrine Disruptor Screening Program (EDSP) Team is currently conducting the studies needed to validate the endocrine disruptor screening and testing methods. To this end, EPA is using the general principles and process developed by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). EPA tasks include:

- Method Development
  - Comprehensive literature review

- Develop initial protocol
- Prevalidation
  - Demonstration of relevance
  - Preliminary data on reliability
  - Standardization of protocol
- Validation on multiple laboratories
  - Proof of relevance and reliability
- Scientific Peer Review
  
- Regulatory Acceptance and Implementation

### Statutory Authorities

The 1996 Food Quality Protection Act (FQPA) and the 1996 Amendments to the Safe Drinking Water Act (SDWA) require EPA to:

*Develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effect as the Administrator may designate.*

The two acts target different sets of chemical substances. Section 304 of the FQPA states that in carrying out the program, the Administrator shall:

*(A) Provide for the testing of all pesticide chemicals; and (B) provide for the testing of any other substance that may have an effect that is cumulative to an effect of a pesticide chemical if the Administrator determines that a substantial population may be exposed to such a substance.*

Section 136 of the SDWA Amendments states that:

*In addition to the substances referred to in (FQPA), the Administrator may provide for testing under the screening program authorized by (FQPA) for any other substance that may be found in sources of drinking water if the Administrator determines that a substantial population may be exposed to such substance.*

In addition, the Toxic Substances Control Act and the Federal Insecticide, Fungicide, and Rodenticide Act provide testing authority that might be applicable to endocrine disruption. A brief summary of the applicable sections of other statutes is provided below:

**FFDCA** - The Federal Food, Drug, and Cosmetics Act (FFDCA) section 408(p) provides EPA authority to require testing of all pesticide chemicals. It also provides EPA authority to require testing of any other substance that might have an effect that is cumulative to an effect of a pesticide chemical if EPA determines that a substantial population might be exposed to the substance. 21 U.S.C. 346(a)(p).

**SDWA** - The Safe Drinking Water Act (SDWA) provides EPA with authority to require testing of any substance that might be found in sources of drinking water if EPA determines that a substantial population might be exposed to the substance. 42 U.S.C. § 300j-17.

**TSCA** - The Toxic Substances Control Act (TSCA) provides authority for EPA to require testing of TSCA chemicals, provided certain hazard and/or exposure-based findings are made. 15 U.S.C. § 2603. In addition, EPA has authority to issue consent orders to require testing when interested parties agree on an acceptable testing program. 51 Fed. Reg. 23706 (June 30, 1986).

**FIFRA** - The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provides EPA with authority to require testing of pesticides if EPA determines that additional data are required to maintain in effect an existing registration. 7 U.S.C. § 136a(c)(2)(B).

## References

Campbell, Neil A. Biology, third edition. California: The Benjamin/Cummings Publishing Company, Inc., 1993.

[Back to Top](#)

# Endocrine Disruptor Screening Program History

## August 1996: Statutory Authorities

In August 1996, Congress passed both the Food Quality Protection Act (FQPA) and amendments to the Safe Drinking Water Act (SDWA), both containing provisions calling for the screening and testing of chemicals and pesticides for possible endocrine disrupting effects. These laws require EPA to develop a screening program that uses appropriate validated test systems and other scientifically relevant information and determine if the effect that certain substances have in humans is similar to the effect produced by a naturally occurring hormone.

Read more about the [Food Quality Protection Act](#) [PDF, 50pp., 253KB, [About PDF](#)]

Read more about the [Federal Food, Drug, and Cosmetic Act Amendments](#) [EXIT Disclaimer](#)

Read more about the [Safe Drinking Water Act Amendments](#) [EXIT Disclaimer](#)

## October 1996: EDSTAC Convenes

The Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), a federal advisory committee, was formed in 1996 to make recommendations on how to develop the screening and testing program called for by Congress. Representatives from industry, government, environmental and public health groups, worker safety groups, and academia comprised EDSTAC. The members of EDSTAC were tasked with developing consensus-based recommendations for a screening program that would provide EPA with the information needed to make regulatory decisions about chemicals that disrupt endocrine system.

EDSTAC thoroughly reviewed and discussed the scientific information available about endocrine disruptors and sought the opinion of other experts and members of the public during its 2-year deliberations. EDSTAC presented its final report to EPA in September 1998.

Read more about the [creation of EDSTAC](#) and its participants.

Read the [EDSTAC Final Report](#)

## August 1998: Federal Register Notice - EDSP

EPA outlined into the Endocrine Disruptor Screening Program (EDSP), which incorporated many of EDSTAC's recommendations, in an August 1998 Federal Register Notice. This notice provides operational details regarding the major elements of EPA's Endocrine Disruptor Screening Program.

Read the [August 1998 FR Notice](#) [PDF, 4pp., 34KB, [About PDF](#)]

## December 1998: Federal Register Notice - Proposed Statement of Policy

In this notice, EPA provides additional details on the Endocrine Disruptor Screening Program. This notice describes the major elements of EPA's EDSP, as well as its implementation.

Read the [December 1998 FR Notice](#) [PDF, 28pp., 228KB, [About PDF](#)]

**July 1999: Federal Register Notice - Proposed Statement of Policy**

At the request of EPA, a joint subcommittee of the EPA Science Advisory Board (SAB) and the FIFRA

Scientific Advisory Panel (SAP) reviewed a set of scientific issues related to the development of the Agency's EDSP.

Read the [1999 SAB/SAP Report: Review of the EPA's Proposed Environmental Endocrine Disruptor Screening Program](#) [PDF, 48pp., 1MB, [About PDF](#)]

**December 1999: NRDC Settlement Agreement**

EPA and the Natural Resources Defense Council (NRDC) entered into an agreement to settle part of a lawsuit that NRDC filed against EPA regarding implementation of the Endocrine Disruptor Screening Program. In the settlement agreement, EPA agreed, among other things, to use best efforts to complete validation of certain screening and testing methodologies that are proposed for use in the program by specific dates, and to use best efforts to start requiring screening and testing of certain chemicals by specific dates.

Read the [Signed NRDC Settlement Agreement](#) [PDF, 16pp., 871KB, [About PDF](#)]

**August 2000: Report to Congress - EDSP Implementation Progress**

EPA presented a Report to Congress in August 2000 summarizing endocrine disruptor issues and describing the Endocrine Disruptor Screening Program. EPA also described its progress in implementing the program, ongoing studies relating to endocrine disruptors, and the measures being taken to address animal welfare concerns under the EDSP.

Read the [2000 Report to Congress](#) [PDF, 20pp., 88KB, [About PDF](#)]

**October 2001: EDMVS/FACA Convenes**

The Endocrine Disruptor Methods Validation Subcommittee (EDMVS) was established under the EPA's National Advisory Council for Environmental Policy and Technology (in accordance with the Federal Advisory Subcommittee Act (5 U.S.C. App. 2 Section 9c)). EDMVS provides advice and counsel to EDSP on scientific issues associated with the validation of Tier 1 and Tier 2 assays on topics including the development and choice of initial protocols; prevalidation study designs, validation study designs, and the integration of prevalidation and validation study results into EDSP Tier 1 and Tier 2 methods documents suitable for external peer review (63 FR 71542).

Read the [EDMVS Mission Statement](#) [PDF, 2pp., 8KB, [About PDF](#)]

**May 2002: Report to Congress - EDVMS Progress**

In a Report to Congress, EPA provided an update on the progress of EDVMS and described validation processes that incorporated the advice of the EDMVS. It also summarized recent subcommittee meetings and presented a list of subcommittee members.

Read the [2002 Report to Congress](#) [PDF, 6pp., 19KB, [About PDF](#)].

Read [Attachment A to the report](#) [PDF, 9pp., 24KB, [About PDF](#)].

**December 2002: Federal Register Notice - Proposed Chemical Selection Approach for Initial Round of Screening**

EPA set forth for public comment the [Proposed Chemical Selection Approach for Initial Round of Screening](#) [PDF, 19pp., 119KB, [About PDF](#)] which presents the approach EPA intends to use for selecting the first group of chemicals to be screened in the Agency's Endocrine Disruptor Screening Program (EDSP).

**June 2004: EDMVAC Established**

The [Endocrine Disruptor Methods Validation Advisory Committee \(EDMVAC\)](#) was established in accordance with the Federal Advisory Committee Act (5 U.S.C. App. 2 Section 9c) and was formed to replace EDMVS. The EDMVAC will continue to function like EDMVS by providing advice and recommendations to EPA on scientific and technical aspects of the Tier I screens and Tier II assays being considered for the Endocrine Disruptor Screening Program. The committee will evaluate relevant scientific issues, protocols, data, and interpretations of the data for the assays

during the validation process. EDMVAC will also provide advice on the composition of the Tier I screening battery.

Read the [EDMVAC Charter](#) [PDF, 3pp., 20KB, [About PDF](#)]

### **September 2005: Federal Register Notice - Chemical Selection Approach for Initial Round of Screening**

EPA published the [Chemical Selection Approach for Initial Round of Screening](#) [PDF, 17pp., 125KB, [About PDF](#)] which presents the approach EPA intends to use for selecting the initial group of 50 to 100 chemicals to be screened under Tier 1 of the Agency's Endocrine Disruptor Screening Program (EDSP).

### **Today: 3 Workgroups/Teams**

EPA is currently implementing EDSP on three fronts:

- Establishing procedural rules and policy for program implementation.
- Developing a strategy for how to prioritize chemicals for screening and testing.
- Developing protocols to conduct specific assays, evaluating their effectiveness, and ensuring that the assay can be performed reliably and consistently in different laboratories.

More information on each of the three fronts is available through the following links.

Read more about [Regulatory Activities](#)

Read more about [Priority Setting](#)

Read more about [Assay Development and Validation](#)

[Back to Top](#)

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