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ENDOCRINE DISRUPTORS
UPDATE

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ENDOCRINE DISRUPTORS

UPDATE

INTRODUCTION

Scientific research is increasingly highlighting the close links between human beings and their environment. Every day, it becomes clearer that the quality of the air, water and soil has a direct impact on the food chain and thus on human beings who are situated at the top of the pyramid. For a few years now, endocrine-disrupting substances – or endocrine disruptors – have become a source of concern. Scientific studies carried out in Canada and in several other countries have shown that those substances can act on the endocrine system of certain invertebrates, fish and higher animals in general. Endocrine disruptors can affect reproduction, growth and development in several species. Scientists are therefore concerned by the role these substances might play in the appearance or increase of hormonal system diseases in human beings, particularly the still-unexplained increase in the incidence of cancers, infertility and malformations of reproductive organs noted in several countries.

The mechanisms through which endocrine disruptors interfere with the hormonal system are complex and not yet well understood. Researchers do know, however, that a wide range of substances affect health, precisely because of the complexity of the hormonal system, and that very low concentrations are sufficient to affect the physiological processes of several animal species.

The extent of disruptors' effects on human beings is still being debated, as many factors limit research and prevent researchers from drawing conclusions as easily as they do for wildlife. Be that as it may, the Canadian government gives this emerging international issue a high priority, recognizing the need to produce the knowledge necessary for informed policy and regulatory decisions.

This document attempts to provide an update on the question of endocrine disruptors. The first part reviews how the endocrine system works, explains what endocrine disruptors are, and how they act in the human body. The second part of the paper introduces some of the substances that could be endocrine disruptors, while the third part discusses the effects of endocrine disruptors on animals and presents the scientific community's various points of view as to the extent of these effects on human beings. Finally, it examines the Canadian government's most recent efforts to control endocrine disruptors.

THE ENDOCRINE SYSTEM AND ENDOCRINE DISRUPTORS: BASIC CONCEPTS

A. How the Endocrine System Works

The endocrine hormone system plays a key role in growth and sexual development. It consists of the endocrine glands, including the testicles, the ovaries, the thyroid, the pancreatic and adrenal glands, the parathyroids and the pituitary gland (which controls the other endocrine glands). These glands secrete substances known as hormones, which are chemical messengers released directly into the bloodstream, where they travel to and stimulate other organs (or receptors). The pancreas, the thyroid, the parathyroids and the pituitary secrete protein hormones; the adrenal glands and the gonads[1] secrete steroid hormones.

Hormones are crucial to morphology, metabolism, blood circulation and the nervous system (which itself affects hormone secretion),[2] and thus help maintain the individual's physiological balance.

B. Endocrine Disruptors and their Impact on the Endocrine System

When hormone secretion is disrupted, a physiological imbalance occurs that can lead to such problems as obesity, diabetes and decalcification of the bones. The natural or artificial substances that may cause this imbalance are described as *endocrine disruptors*. Disruptors are divided into three categories:

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(1) Testicles and ovaries.

(2) *Petit Larousse de la médecine*, Tome 1, 1976.

- **Mimics** – These disruptors are perceived by the body as genuine hormones because they elicit the same chemical reactions as natural hormones.

- **Blockers** – These disruptors, by blocking the cell receptors, prevent naturally occurring hormones from affecting cells in the usual way.

- **Triggers** – These disruptors elicit unusual or abnormal reactions in cells.(3)

For example, if we look at the development of a child from an embryonic stage to birth, the entire process is regulated by specific chemical messengers that are programmed to be released at one point and taken up at another in precise concentrations and at specific times. If a chemical interferes with these messengers, irreversible damage can result at some stage. The effects may include changes in the development and function of the reproductive system, which in turn produces abnormalities, including deformities.

The effects of endocrine disruptors are not limited to male or female sex hormones; they also affect other endocrine glands that play a role in growth, development and reproduction.(4)

SUBSTANCES THAT CAN ACT AS ENDOCRINE DISRUPTORS

A. Pollution: A Source of Endocrine Disruptors

The scientific community clearly recognizes that a wide range of substances interfere with the natural chemical messengers in animals.(5) These substances are present throughout the environment, and even if we do not yet know the extent of their effect on the human endocrine system, the human organism is nevertheless in almost constant contact with them. That is due, in particular, to the fact that a large number of these substances can easily be transported by the wind in particle or droplet form, and may travel thousands of kilometres from their source. Rain then deposits the particles on soil or in waterways, where they accumulate and undergo transformation. They are then absorbed by vegetation and end up in the food chain,

(3) The Endocrine Disrupter Resource Center, Institute for Agriculture and Trade Policy (http://www.iatp.org/edrc/About.cfm).

(4) Environment Canada, *Endocrine Disrupting Substances in the Environment*, 2000.

(5) *Ibid*.

after which they become concentrated in the fatty tissue of animals. The movement of substances over long distances seems to be confirmed by a study of Inuit infants in Nunavik and Baffin Island, which found that babies born in this region are exposed to higher levels of certain products (such as PCBs) than are babies born in southern Canada.(6) Variations in exposure to these pollutants are attributable primarily to diet, although sociodemographic differences also come into play.

Environment Canada has established that several substances present in the environment may act as endocrine disruptors (see Table 1). For instance, the presence of industrial, agricultural and municipal waste in the environment may expose organisms to abnormally high doses of natural substances such as sexual hormones or phyto-estrogens (plant by-products or derivatives). Synthesized chemical products such as pesticides, the by-products of industrial activity (dioxins, furans), and industrial wastes (PCBs) can also affect the normal functioning of the endocrine system.

The U.S. Endocrine Disrupter Resource Center has identified about 50 of these substances (see Appendix 1). According to that organization, very minute concentrations (parts per trillion) of these products in an organism would be enough to affect its endocrine system. Half of the substances mentioned in the Center's list are part of the organochlorine group: a description of that group is provided later in this paper.

(6) Gina Muckle, Éric Dewailly and Pierre Ayotte, "Prenatal exposure of Canadian children to polychlorinated biphenyls and mercury," *Canadian Journal of Public Health*, Vol. 89, Suppl. 1, May/June 1998, pp. 22-26.

TABLE 1: SOURCES, CATEGORIES AND EXAMPLES OF SUBSTANCES THAT HAVE BEEN REPORTED AS POSSIBLE ENDOCRINE DISRUPTORS

Examples of Sources	Categories (Example of Uses)	Examples of Substances
Incineration, landfill	Polychlorinated Compounds (from industrial production or by-products of mostly banned substances)	Polychlorinated dioxins, polychlorinated biphenyls
Agricultural runoff / Atmospheric transport	Organochlorine Pesticides (found in insecticides, many now phased out)	DDT, dieldrin, lindane
Agricultural runoff	Pesticides currently in use	Atrazine, trifluralin, permethrin
Harbours	Organotins (found in antifoulants used to paint the hulls of ships)	Tributyltin
Industrial and municipal effluents	Alkylphenols (Surfactants – certain kinds of detergents used for removing oil – and their metabolites)	Nonylphenol
Industrial effluent	Phthalates (found in placticisers)	Dibutyl phthalate, butylbenzyl, phthalate
Municipal effluent and agricultural runoff	Natural Hormones (produced naturally by animals); synthetic steroids (found in contraceptives)	17-b-estradiol, estrone, testosterone; ethynyl estradiol
Pulp mill effluents	Phytoestrogens (found in plant material)	Isoflavones, lignans, coumestans

Source: Environment Canada, *Endocrine Disrupting Substances in the Environment*, 2000.

Some scientists suspect that ordinary products used in everyday life may also be endocrine disruptors. Possible examples include cleaning products, beauty products and compounds produced by the breakdown of plastics.

News reports and newspaper articles tell startling stories that link chemical substances and diseases related to the disruption of the hormonal system such as breast cancer and non-Hodgkin's lymphoma. For instance, some researchers suggest that plastics, fuels and certain drugs or pesticides may stimulate excessive hormone secretion and thus accelerate the development of cancer in a given gland or the organ it affects. More than anything, these news reports reflect the population's growing concern with the effects of pollution on health.

B. Persistent Organic Pollutants

Until recently, most research work on endocrine disruptors has been done on persistent, bioaccumulative and toxic substances, many of which are mentioned in Table 1 (dioxins, PCBs, organochlorine pesticides, etc.). Those chemical substances – persistent organic pollutants (POPs) – come into the environment as a result of human activities, and their list will probably continue to grow.

POPs share three broad characteristics:

- **persistent**: POPs are called *persistent* because they resist degradation in normal environmental conditions.
- **liposoluble**: POPs are also *liposoluble* and very slightly water-soluble, which means that the organism cannot excrete them, which is why they accumulate in tissue. The accumulation of a contaminant over time within one organism is known as *bioaccumulation*. The organism that eats plants or animals that have already been contaminated can accumulate a high concentration of contaminants, and that concentration increases with every step up the food chain. This increase in the concentration of POPs as you go up the food chain is known as *bioamplification*.(7)
- **semi-volatile**: POPs are *semi-volatile*, i.e., they move easily from a solid state to a gaseous state at high temperatures and become solid again if temperatures drop. Used in southern regions, these products partly evaporate and are transported by the wind; they then condense when they come in contact with cold arctic air and settle on the ground. When these pollutants reach the North (all of the territory north of the 60th parallel, i.e., the sub-arctic and arctic regions), they tend to accumulate because the low temperatures are not conducive to evaporation. POPs can repeat that cycle several times and over long distances, which has caused this phenomenon to be known as the “grasshopper effect.”

(7) *Presentation concerning pesticide residues in the Canadian Arctic and the Northern Contaminants Program*, House of Commons Standing Committee on the Environment and Sustainable Development, 9 December 1999.

Because of this travel over long distances allied to their particular physical and chemical characteristics, POPs affect arctic regions in particular.(8) According to the literature, 80% of pollutants in the Arctic are thought to be from countries other than Canada.(9)

Although the use of most POPs is prohibited or restricted in Canada, they are produced, used or discharged in a number of other countries; and because POPs are readily transportable by air, they can still put the Canadian population (and that of many other countries) at risk. That is why they are covered by international agreements adhered to by Canada. These agreements currently cover the following 16 POPs. Most of these pollutants are in *organochlorines* – organic substances that contain chlorine atoms; 11 of them are pesticides.

- **Pesticides:** Chlordane, DDT, aldrin, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, chlordecone, lindane and toxaphene.
- **Industrial chemical products:** PCBs, hexabromobiphenyl.
- **Contaminants:** Dioxins, furans, polycylic aromatic hydrocarbons (PAH).

C. Heavy Metals

Canada has included three heavy metals – cadmium, mercury and lead (see Appendix 2) – in its research programs on the effects of toxic substances on health and on the endocrine system in particular. Those three metals are thought to act as endocrine disruptors and are among the substances being studied under the Northern Contaminants Program sponsored by Indian and Northern Affairs Canada (see Appendix 3).

These three metals are present in the environment as a result of various natural processes. However, since the beginning of the industrial era, human activity has raised the levels of these metals in natural ecosystems, and as result of bioaccumulation and bioamplification, in the food chain.

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(8) J. Jean, K. Adare and R. Shearer, *Canadian Arctic Contaminants Assessment Report*, Northern Contaminants Program, Indian and Northern Affairs, 1997; Draft of the report of the *EcoSummit* 1999 conference.

(9) Brief submitted by the Inuit Tapirisat Circumpolar Conference of Canada to the Standing Committee on Environment and Sustainable Development, 9 December 1999.

D. Organochlorines

Organochlorines are chemical products containing both carbon and chlorine. They are used for a variety of purposes including pesticides, refrigerants or other industrial products. Some organochlorines, such as dioxins and furans, are by-products of (various) industrial processes that are released into the environment, and several of them are believed to be endocrine disruptors (Table 1). Many of them are POPs that are now prohibited in Canada, but traces of them can still be found in the environment. They may even reach high concentrations in the tissues of predators at the top of the food chain.

In Canada, the double-crested cormorant (a fish-eating predator) is used as a national indicator of persistent organochlorine levels because of its broad distribution across southern Canada, especially in areas of concentrated human activity.(10)

E. Pesticides

The first pesticides,(11) which appeared during the 1940s, contained mostly organochlorines. They were used in an intensive way – both in agriculture and forest management, as well as to protect wooden buildings and health – in order to control a variety of insects. Thus, it is not surprising to learn that because of their characteristics, traces of organochlorine pesticides still persist in the environment, even if several other groups of chemicals have replaced them, at least in Canada, where more than 50 million kilograms of herbicides, insecticides and fungicides are used each year.(12)

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(10) Environment Canada, "Persistent organochlorines," *S and E Bulletin*, January 1998, Environment Canada Internet site (http://www.ec.gc.ca).

(11) A pesticide is any product designed to limit, destroy, attract or repel pests that is used, sold or imported into Canada. Pesticides include chemicals, devices and even organisms. Pest control products include herbicides, insecticides and fungicides as well as algicides, animal and insect repellants, cleaning and antimicrobial products, preservatives for materials and wood, and devices for the control of insects and rodents. This definition is based on the definition of *control product* in the *Pest Control Products Act*.

(12) World Wildlife Fund, *The Problems with Pesticides in Canada*, a Briefing Book for Parliamentarians, Canada, June 1999.

F. Other Substances

After having focused almost exclusively on persistent, bioaccumulative and toxic substances, scientists today are studying substances that may not persist as long in the environment, but are nevertheless widespread. They may affect growth, development and reproduction of organisms, even in low concentrations. These are substances that are found in municipal and industrial effluents as well as in the runoff from agricultural lands, natural plant estrogens, chemical products such as alkyphenols and tributyltin (Table 1), and certain other ingredients of pesticide formulations.(13)

THE EFFECTS OF ENDOCRINE DISRUPTORS: THE SCIENTIFIC POINT OF VIEW

A. Effects on Animals and Humans

Canada has been a pioneer in research on endocrine disruptors, thanks in particular to the efforts of the Canadian Wildlife Service, whose work highlighted cases of disruption of the endocrine system in animals.(14) Research showed effects on the reproduction and development of fish and birds (Table 2); the observation of embryonic malformations in various species and of the mortality of such embryos confirmed embryotoxic effects(15) and teratogenic(16) of certain pollutants. The research noted various anomalies: a decrease in the size of the penis and testicles, a decline in sperm counts, reproductive anomalies, feminization of males, and masculinization of females.

(13) Environment Canada (2000).

(14) Standing Committee on Environment and Sustainable Development, *PESTICIDES: Making the Right Choice for the Protection of Health and the Environment*, May 2000.

(15) Embryotoxic: The character of a substance that can harm the embryo.

(16) Teratogenic: The character of a substance that can cause abnormal or monstrous forms in an organism.

TABLE 2: SOME EXAMPLES OF ENDOCRINE-RELATED EFFECTS IN WILD POPULATIONS

- Deformities and embryo mortality in birds and fish caused by exposure to industrial chemicals and organochlorine insecticides.
- Impaired reproduction and development in fish exposed to effluents from pulp and paper mills.
- Abnormal reproduction in snails exposed to antifouling substances applied to the exteriors of ships.
- Depressed thyroid and immune functions in fish-eating birds.
- Feminization of fish near municipal effluent outlets.

Source: Environment Canada, *Endocrine Disrupting Substances in the Environment*, 2000.

These results have blazed a trail for the world scientific community, which is now studying the issue of active compounds in the environment in relation to the human population. Over the past three decades, many countries have witnessed an increase in diseases related to malfunctions of the endocrine system (thyroid dysfunction, infertility, defects and cancer of the reproductive organs).(17) In Canada, Ontario has experienced an apparent 2% increase each year in the incidence of testicular cancer (60% over the past 30 years);(18) and as early as 30 years ago, endocrine disruptors were being suggested as a possible cause.(19) Recent studies suggest that these substances also have an effect on the human body; for instance, women who drank water daily from Lake Michigan in the 1970s are reported to have been exposed to persistent toxins and to have given birth to neurologically damaged babies.(20) The learning ability and behaviour of the children with the highest exposure levels are believed to have been irreversibly affected.

(17) The Endocrine Disrupter Resource Center, Institute for Agriculture and Trade Policy (http://www.iatp.org/edrc).

(18) *Ibid*.

(19) Shirley A. Briggs, *Basic Guide to Pesticides – Their Characteristics and Hazards*, Rachel Carson Council, 1992.

(20) Michael Gilbertson, "Linking Water Quality to Wildlife and Human Health," *FOCUS*, International Joint Commission, November 1998, pp. 18-19.

Similar conclusions were reached in a 1990 study of babies in New York whose mothers had consumed fish from Lake Ontario in the 1980s while pregnant.(21)

There is a great deal of debate concerning research on the human population, in particular because scientists do not agree on the extent of the problem. A partial list of recent studies suggests four main conclusions in connection with endocrine disruptors:

- Several studies conclude that more in-depth research is essential to a thorough understanding of endocrine disruptors.
- Some studies indicate that most of the studied products appear to have at least some impact on mammals (including humans).
- Other studies suggest that the effects of endocrine disruptors are seen primarily in fetuses and developing children.
- Other studies suggest that the extent of the effects varies according to a host of parameters that are distinct from the effect of the products studied.

B. Effects on the Reproductive and Endocrine Systems

Many authors agree that the pollutants being studied can affect the endocrine system by coming between the hormones and hormone receptors (paralyzing or triggering disruptors). Benjamin Danzo is among those who support this view.(22) His work on such products as DDT congeners,(23) dieldrin, atrazine and pentachlorophenol has led him to observe that these substances interfere to varying degrees with the binding of ligands(24) to steroid receptors and binding proteins.

A Danish study of 18 organochlorine products has linked the incidence of breast cancer to pesticides and has shown that some organochlorines may have a slight estrogenic

(21) International Joint Commission, *FOCUS* (http://www.ijc.org/focus).

(22) Benjamin J. Danzo, "Environmental Xenobiotics May Disrupt Normal Endocrine Function by Interfering with the Binding of Physiological Ligands to Steroid Receptors and Binding Proteins," *Environmental Health Perspectives*, Vol. 105, No. 3, March 1997, pp. 294-301.

(23) Congener: A product that belongs to the same chemical group and is derived from the same initial compound.

(24) Ligand: In this case and in non-technical terms, a molecule that has the necessary properties to attach itself to a receptor.

effect.[25] In addition, some chemical pollutants with limited ability to stimulate hormones may become more active (mimics) in synergy with other products. In fact, Steven Arnold and various other researchers have hypothesized that estrogen receptors have more than one site that can bind with pollutants.[26] This is the case with chlordane, which has no effect on the endocrine system by itself, but can make dieldrin more potent.[27] However, other researchers have been unable to demonstrate this type of synergy;[28][29] these divergent observations further complicate the subject of endocrine disruptors and the extent of their effects.

C. Heightened Effects on the Fetus

Research was undertaken after scientists in many countries had observed a decrease in sperm counts and an increase in diseases affecting male genital organs. This research suggests that, in such cases, there may have been exposure to chemical pollutants that act like hormones in the fetal stage or in early childhood, and that the effects are observed in adulthood. A literature review reported on that hypothesis when male fetuses were inadvertently exposed (via the mother) to abnormal doses of synthetic estrogens such as diethylstilbestrol (a synthetic hormone used for the treatment of ovarian dysgenesis and prostate cancer).[30]

The greater sensitivity of fetuses and children to toxins present in the environment is attributable to their rapid growth and their physiological and metabolic immaturity. The fact

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(25) Annette Pernelle *et al.*, "Organochlorine Exposure and Risk of Breast Cancer," *The Lancet* 352(9143), 1998, pp. 1816-1820.

(26) Steven Arnold *et al.*, "*In Vitro* Synergistic Interaction of Alligator and Human Estrogen Receptors with Combinations of Environmental Chemicals," *Environmental Health Perspectives*, Vol. 105, Suppl. 3, April 1994, pp. 615-618.

(27) Steven Arnold *et al.*, "Synergistic Activation of Estrogen Receptor with Combinations of Environmental Chemicals," *Science*, Vol. 277, 1997, pp. 462-463.

(28) K.F. Arcaro *et al.*, "Lack of Synergy by Mixtures of Weakly Estrogenic Hydroxylated Polychlorinated Biphenyls and Pesticides," *Environmental Health Perspectives*, Vol. 106, Suppl. 4, August 1998, pp. 1041-1046.

(29) K.F. Ramamoorthy *et al.*, "Estrogenic Activity of a Dieldrin/Toxaphene Mixture in the Mouse Uterus, MCF-7 Human Breast Cancer Cells, and Yeast-Based Estrogen Receptor Assays: No Apparent Synergism," *Endocrinology*, Vol. 138, No. 4, April 1997, pp. 1520-1527.

(30) Jorma Toppari *et al.*, "Male Reproductive Health and Environmental Xenostrogens," *Environmental Health Perspectives*, Vol. 104, Suppl. 4, August 1996, pp. 741-803.

that children absorb larger quantities of air, food and fluids than do adults, relative to their body mass, also increases their potential for overexposure, as compared to adults.(31)

D. Non-estrogenic Effects

Research does not always confirm that pollution has hormonal effects on living organisms; according to some findings, chemical pollutants have only a minor impact on the endocrine system while, according to others, the pollutants may harm health through mechanisms independent of the hormone receptors.

W.G. Foster,(32) for instance, has questioned whether there is real cause for concern about these disrupting environmental agents, in view of two factors: 1) the products (in the case of this study, POPs) have only a minor impact on the hormone system and 2) these products act through mechanisms that are independent of the estrogen receptor. On the basis of his work, he concluded that further studies must resolve a number of points before this question can be answered, but emphasized that current literature suggests that the potential effects of chemical pollutants on public health should be a matter of concern.

E. The Need for More Information

Scientists agree on at least one point: the current data on endocrine disruptors are inadequate. More comprehensive studies of the endocrine system and toxic substances must be conducted to establish clearly the scope of the problem and to develop a strategy for prevention and intervention.(33) Every scientist has his or her own view of what must be done.

According to Tracey M. Slayton, among others, science must compile more information on how pollutants act, the biological significance of the observed effects (reversible

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(31) Graham W. Chance and Eef Harmsen, "Children are Different: Environmental Contaminants and Children's Health," *Canadian Journal of Public Health*, Vol. 89, Suppl. 1, May/June 1998, pp. 10-14.

(32) Warren G. Foster, "Endocrine Disruptors and Development of the Reproductive System in the Fetus and Children: Is there a cause for concern?" *Canadian Journal of Public Health*, Vol. 89, Suppl. 1, May-June 1998, pp. 41-45.

(33) Danzo (1997); Thomas M. Crisp *et al*., "Environmental Endocrine Disruption: an Effects Assessment and Analysis," *Environmental Health Perspectives*, Vol. 106, Suppl. 1, February 1998, p. 11-56; Toppari *et al.* (1990); Tracey M. Slayton, "Persistent Toxins that Bioaccumulate (PTbs) and Endocrine Disruptors," Internet site, 1996; Helen Tryphonas, "The Impact of PCBs and Dioxins on Children's Health: Immunological Considerations," *Canadian Journal of Public Health*, Vol. 89, Suppl. 1, May/June 1998, pp. 54-57.

or irreversible), the dose-response relationship, and the potential for chemical interaction (for example, observation of synergistic or antagonistic effects between estrogens and toxic compounds). Thomas Crisp and his team focus on the imbalance in the central nervous system and the pituitary integration(34) of hormonal and sexual activity, the male and female reproductive systems, and thyroid function. Their results suggest the need for analysis of the potential of the endocrine disruptors to induce prostate, breast and testicular cancer and their impact on endometriosis. In addition, attention is drawn to the importance of a better understanding of the etiology(35) of the diseases that are attributed to pollutants.

With regard to specific research on the developing fetus and the newborn, research seems to be needed on the following points: the developmental stage (which is most sensitive to exposure); thyroid function, including steroid-dependent processes as other than estrogen-dependent effects; and the combination of chemical products present in the environment.

The Endocrine Disrupter Screening Program, established in 1998 by the U.S. Environmental Protection Agency (EPA),(36) offers the hope of additional scientific data, and perhaps more systematic data. The program is designed to target pesticides and other chemical substances that act – or are presumed to act – in humans in the same way as natural hormones. It will first examine the effects of some of these products on the three best-known hormone systems (estrogen, androgen and thyroid systems), in order to: determine whether these effects are similar to those produced by the hormones in question; describe those effects; and quantify the effects. This work should allow for the classification of products based on their capacity to simulate hormones. Later, the research could target other hormonal systems.

RECENT GOVERNMENT MEASURES IN CANADA

A. National Initiatives

The problem of endocrine disruptors is complex, and finding solutions requires the participation of governments as well as industries, universities and the public. Under the terms of the new *Canadian Environmental Protection Act* (*CEPA*), the Canadian government has

(34) Pituitary: site at which hormones are transferred from the hypothalamus to the pituitary circulation.

(35) Etiology: the study of the causes of disease and factors contributing to it.

(36) Environmental Protection Agency, “Endocrine Disruptor Screening Program – Notice” (http://www.epa.gov/opptint/opptendo), 11 August 1998.

set up a research investment fund, one part of which deals specifically with endocrine disruptors. The Toxic Substances Research Initiative (TSRI) subsidizes research in specific areas of environment and health, including toxic substances that disrupt the hormonal system.(37) The TSRI is overseen by a Scientific Management Committee made up of government and non-governmental scientists specialized in the area of toxic substances. The Initiative is a result of a partnership between the departments of Health, Environment, Fisheries and Oceans, Natural Resources, Indian and Northern Affairs, and Agriculture and Agri-food.

Environment Canada incorporates research on endocrine disruptors into its multiple regional projects on ecosystems, which allows it to increase what is known on the effects of endocrine disruptors present in the environment. In addition to other tasks, the Department is drawing up environmental assessment protocols to be used in the field and in laboratories. Moreover, it is developing its national leadership by putting information tools – including an Internet site and a recently created Fact Sheet on the topic of endocrine disruptors – at the disposal of scientists, decision-makers and the general population.

Canada has taken several other measures (see Appendix 3); if they do not apply directly to endocrine disruptors, they will nevertheless allow for the gathering of information on toxic substances that could eventually be targeted.

B. International Initiatives

The Canadian government is working with international organizations in order to address the issue of endocrine disruptors as part of a list of serious world problems. These organizations include the Organisation for Economic Co-operation and Development (OECD), the United Nations Environment Program (UNEP), and the North American Free Trade Agreement Commission for Environmental Cooperation (NAFTA-CEC). Among other initiatives, Environment Canada will participate in international activities involving the global harmonization of assessment methods designed to help in the fight against endocrine-disrupting products.

Table 3 summarizes the international accords that Canada has ratified or is in the process of ratifying to solve the global problem posed by POPs. One of those accords, prepared

(37) Environment Canada, “Federal Ministers Announce that $40 million will be allocated to research on health and environment in Canada,” Communiqué, 7 December 1998.

under the auspices of UNEP, should be ready in the year 2000. This is a legally binding instrument for implementing international action on certain organic pollutants; its purpose is to reduce emissions and releases of substances such as DDT, toxaphenes and PCBs that accumulate in the environment, particularly in the Arctic. During the first session of the Intergovernmental Negotiation Committee, in June 1998, the delegates from 92 countries defined the principles that were to guide its preparation.

TABLE 3: NATIONAL AND INTERNATIONAL MEASURES TAKEN BY CANADA ON TOXIC SUBSTANCES

Substances	UN-ECE Treaty on POPs	UN-ECE Treaty on heavy metals	TSMP (Track 1)	Treaty UNEP on POPs	NAFTA-CEC
Chlordane	x		x	x	x
DDT	x		x	x	x
PCBs	x		x	x	x
Aldrin	x		x	x	
Dieldrin	x		x	x	
Endrin	x		x	x	
Heptachlor	x		x	x	
Hexachlorobenzene	x		x		(x)
Mirex	x		x	x	
Dioxins	x		x	x	(x)
Furans	x		x	x	(x)
Toxaphene	x		x	x	
Chlordecone	x				
Hexabromobiphenyl	x				
PAHs	x				
Lindane	x				
Mercury		x			x
Cadmium		x			
Lead		x			

Source: The Green Lane, Environment Canada Internet site, October 1998.

(x)	Information from Marcos Silva, CEC Council Session held at Banff, Commission for Environmental Co-operation, e-mail, 28 June 1999
NAFTA-CEC	North American Free Trade Agreement Commission for Environmental Co-operation
UN-ECE	United Nations Economic Commission for Europe
TSMP	Toxic substances management policy (these substances are to be eliminated (quasi-elimination) according to the policy)
UNEP	United Nations Environment Program

In addition, Canada – together with 43 European and North American countries – has signed two protocols on persistent organic pollutants under the auspices of the United Nations Economic Commission for Europe. The first, *New Persistent Organic Pollutants Protocol to the Convention on Long Range TransBoundary Air Pollution*, covers 16 POPs as well as contaminants and derivatives such as dioxins and furans. The second, the *New Heavy Metals Protocol to the Convention on Long Range TransBoundary Air Pollution*, deals with three heavy metals: cadmium, lead and mercury. Canada ratified these agreements on 22 December 1998.(38)

CONCLUSION

Most of the toxic substances suspected of having effects on the hormone system have appeared on the market since World War II; many are pesticides from the organochlorine group. Although available data are not sufficient to determine effects on humans with absolute certainty, research has proven that those substances do act on the endocrine system of animal species. Indeed, hundreds of substances remain to be analyzed, and the conclusions compiled to date are valid only for those products already specifically assessed.

Moreover, although some scientists are extremely concerned about these substances, others are more cautious. In fact, some studies show that a number of additional factors other than endocrine disruptors – such as changes in diet and habits during pregnancy – may be responsible for an increase in the incidence of cancer.

In any event, most researchers agree on one point: more studies must be carried out to provide further information on the effects of endocrine disruptors. This information will then make it possible to establish policies and standards for the assessment and use of clinical products.

Canada is already participating in a number of national and international efforts to counteract the effects of these products on health and the environment. Other possible measures include a review of the current *Pest Control Products Act*, which has not been updated for more than 30 years. In addition, the Canadian government could invest in detailed research on the effect of the endocrine disruptors on the hormone system.

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(38) Environment Canada, “Canada First Country to Ratify International Agreements to Reduce Toxic Airborne Pollutants,” News Release, 22 December 1998.

APPENDICES

APPENDIX 1

LIST OF KNOWN AND SUSPECTED HORMONE DISRUPTORS

A. Pollutants with Widespread Distribution Reported to have Reproductive and Endocrine-disrupting Effects

Persistent Organohalogens

Dioxins and furans	Octachlorostyrene
PCBs	Hexachlorobenzene
PBBs	Pentachlorophenol

Pesticides

2,4,5-T	DBCP	h-epoxide	nitrofen
2,4-D	DDT	kelthane	oxychlordane
alachlor	DDT metabolites	kepone	permethrin
aldicarb	dicofol	malathion	synthetic pyrethroids
amitrole	dieldrin	mancozeb	toxaphene
atrazine	endosulfan	maneb	transnonachlor
benomyl	esfenvalerate	methomyl	tributyltin oxide
beta-HCH	ethylparathion	methoxychlor	trifluralin
carbaryl	fenvalerate	metiram	vinclozolin
chlordane	lindane	metribuzin	zineb
cypermethrin	heptachlor	mirex	ziram

Penta- to Nonyl-Phenols

Bisphenol A

Phthalates

Di-ethylhexyl phthalate (DEHP)	Di-hexyl phtalate (DHP)
Butyl benzyl phthalate (BBP)	Di-propyl phthalate (DprP)
Di-n-butyl phthalate (DBP)	Dicyclohexyl phthalate (DCHP)
Di-n-pentyl phthalate (DPP)	Diethyl phthalate (DEP)

Styrene dimers and trimers

Benzo(a)pyrene

Heavy Metals

Cadmium	Lead	Mercury

B. Pollutants with Widespread Distribution Reported to Bind to Hormone Receptors and Therefore Suspected to Have Reproductive and Endocrine-disrupting Effects

2,4-dichlorophenol
diethylhexyl adipate
benzophenone
N-butyl benzene
4-nitrotoluene

Sources: The list of substances considered to have endocrine-disrupting and reproductive effects is compiled by the Endocrine Disrupter Resource Centre from a variety of sources including:

Colborn, T. and C. Clement. *Chemically Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection.* Princeton, N.J.: Princeton Scientific Publishing, 1992.

Colborn, T., F. vom Saal and A.M. Soto. "Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Humans," *Environmental Health Perspectives*, Vol. 101, No. 5, 1993.

Lyons, G. *Phthalates in the Environment*, World Wildlife Fund, UK, 1995.

Ministry of Agriculture, Fisheries and Food. *Effects of Trace Organics on Fish, Phase II*, Foundation for Water Research, UK, 1995.

Note: All of the substances currently identified as hormone disruptors are now widely distributed throughout the environment; some are common constituents of consumer products, and many are now found in human tissues.

APPENDIX 2

DESCRIPTION OF HEAVY METALS STUDIED BY THE NORTHERN CONTAMINANTS PROGRAM

Cadmium: Cadmium is a white, ductile, malleable metal from the same group as mercury. It is used in alloys to protect other metals. Aside from its use by the metallurgical industry, its most familiar use is in nickel-cadmium batteries. In spite of the fact that the transportation sector, waste disposal activities and land application of sewage sludge also contribute to the presence of cadmium, metal smelters and refineries are the main source of cadmium in the Canadian environment (82%, or 130 t/year); 92% of this metal is found in the atmosphere.(39) Although cadmium does not break down in the environment, chemical and physical processes affect its mobility, its bio-availability and lifetime, and thus the extent of the danger that it presents to mammals and human beings. For example, cadmium has been found to accumulate in the organs of marine mammals (bioaccumulation). According to experts at Environment Canada and Health Canada, current information suggests that in certain cases, the accumulation of cadmium in the environment may have adverse effects on human health. For instance, there has been an increase in mortality attributable to lung cancer in workers exposed simultaneously to cadmium and arsenic. Cadmium is also associated with effects on the renal system.

Mercury: The production of chlorine and caustic soda, waste incineration, coal burning and metallurgy are the principal anthropogenic sources of mercury, a white metal that is liquid at room temperature. The methylated form of mercury accumulates in the environment (bio-amplification), while the gaseous elementary form of the metal found in the atmosphere is increasing globally at a rate of approximately 1% per year.(40) Mercury also accumulates in lake sediments. This metal is associated in particular with sensory or neurological deficits. Dental amalgams made the headlines when it was observed that the mercury they contained could have effects on health. Although current evidence does not indicate that these amalgams are causing illness in the general population, according to a notice issued by Health Canada, a small

(39) Environment Canada and Health Canada, *Cadmium and its compounds*, 1994.

(40) Jensen *et al.* (1997).

proportion of the population can suffer severe health effects from even a low exposure.(41) More detailed studies are required for a proper assessment of this metal and its real effects.

Lead: Lead, an extremely malleable bluish-grey metal, was found primarily in gasoline until the 1975 adoption of regulations to reduce lead additives. Because lead additives have been eliminated in gasoline and in the production of food cans, the principal sources of this pollutant today include industrial emissions (foundries, refineries), plumbing solders, hunting ammunition, certain toys, domestic household products, and food containers. Lead exposure occurs primarily (80% to 90%) through food.(42) Because children absorb more food than do adults in relation to their body mass, they have the highest blood concentrations of lead. Adult men have higher concentrations than do women, because of their slightly higher hemoglobin level. Lead poisoning can harm the hematological, gastrointestinal and neurological systems. Wildlife (particularly waterfowl and their predators) is particularly affected by the lead shot used by hunters; an estimated 250,000 aquatic water birds die each year of lead poisoning. To address this problem, Canada now requires hunters to use non-toxic shot.(43)

(41) Health Canada, *Health Canada Position Statement on Dental Amalgams*, Health Canada Internet site, 30 June 1999.

(42) Jensen *et al.* (1997).

(43) Environment Canada, *Lead Shot*, Fact Sheet, the Green Lane Internet site, Environment Canada, 5 February 1999.

APPENDIX 3

GOVERNMENT MEASURES

Northern Contaminants Program (NCP)

The first phase of the NCP ended in 1997, and its objective is to assess the risk of contamination by various products associated with the traditional foods eaten by Aboriginal people in the arctic region. The program is funded by Treasury Board and four departments that also participate in its management to varying degrees. For instance, Health Canada provides advice on the risks posed by certain POPs and funds research on the analysis of the potential problems associated with those substances. Three heavy metals have been added to the list of substances being studied (see Appendix 2).

Toxic Substances Management Policy (TSMP)

The Toxic Substances Management Policy was adopted in 1995 to provide a scientific context for the identification of toxic substances present in the environment. A two-part or "two track" (according to the Policy) assessment grid is used for the classification of substances:

- "Track-1 substance" – a substance that is bioaccumulative, persistent and primarily the result of human activity, in which case it must be eliminated from the environment ("quasi-elimination") under the terms of the *Canadian Environmental Protection Act* (for example, chlordane, in Table 3, is a Track-1 substance);
- "Track-2 substance" – a toxic or worrisome substance subject to life-cycle management to prevent or minimize, as much as possible, its release into the environment.

New provisions of the *Canadian Environmental Protection Act* (*CEPA*)

Under the terms of the new *CEPA* adopted 14 September 1999, all substances currently in use in Canada will be categorized to determine if they are toxic. *CEPA* also establishes deadlines for measures to be taken to control toxic substances and will require the virtual elimination of the most dangerous of these. These measures will include assessing 23,000

new and existing substances, as well as managing and controlling toxic substances and tracking the progress of the process.(44)

The scope of the Act is illustrated by the story of dioxins (polychlorinated dibenzoparadioxins) and furans (polychlorinated dibenzofurans), which were declared toxic in 1999 under the old *Canadian Environmental Protection Act*, on the basis of an assessment by Environment Canada and Health Canada. These by-products were then added to the list of toxic substances in the Act. The subsequent adoption of various regulations, including the *Pulp and Paper Effluent Regulations* (in 1992), reduced the quantity of dioxins and furans released into the environment by 98%.

Pest Management Regulatory Agency (PMRA)

The PMRA was established in 1995 to apply the *Pest Control Products Act* (*PCPA*). Under this Act, all products imported, manufactured, sold or used in Canada must be federally registered. A pest control product may not be registered unless the risks to human health and to the environment are acceptable and the product is useful for pest control. The *PCPA* also provides a regulatory framework for aquacultural producers, unless the product (parasiticide) is considered a drug, in which case the *Food and Drugs Act* applies.(45)

Various measures relating to heavy metals and chlorinated substances

The *North American Regional Action Plan on Mercury*, initiated by the Commission for Environmental Cooperation of the NAFTA, is now in phase II. This plan is designed to eliminate gradually, or to prohibit, uses of mercury that present unacceptable or uncontrollable risks of release into the environment or risks to health.

The *Canadian Plumbing Code* prohibits the use of lead solder in new plumbing systems and in repairs to drinking water supply systems.(46) In addition, in 1996, Canada adhered to the *Organisation for Economic Co-operation and Development Ministerial Declaration on Lead.* As a result, it is now sharing its skills in monitoring lead exposure with other countries. The Declaration supports the elimination of leaded gasoline as well as ending the exposure of

(44) Environment Canada, "New Funding to Implement the New Canadian Environmental Protection Act," Communiqué, *The Green Lane*, 4 September 1999.

(45) Health Canada, *Food and Drugs Act*, March 1999.

(46) Health Canada, *It's Your Health: Lead and Human Health*, Health Canada Internet site, 28 June 1996.

children to lead through products designed for them and through food containers. The Declaration includes a voluntary action plan for lead-producing industries. For instance, producers are encouraged to reduce lead exposure and to establish risk reduction programs.(47)

The *Chlorinated Substances Action Plan*, adopted by Canada's Ministers of the Environment and Health, presents Canada's approach to chlorinated substances.(48) It consists of five components designed to meet specific objectives: targeting critical uses and products through legislative or voluntary tools; improving scientific knowledge; studying the effects on health and on socio-economic aspects; providing Canadians with better information; and promoting and directing international efforts.

(47) Environment Canada, *Canada Supports OECD Decisions to Reduce Lead Exposure and Green Government Operations*, The Green Lane, Environment Canada Internet site, 5 February 1999.

(48) Environment Canada and Health Canada, *Chlorinated Substances Action Plan*, Progress Report, Environment Canada Internet site, October 1996.