

The endocrine system and EDCs

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Moving forward in the face of uncertainty





The Strategic Approach to International Chemicals Management (SAICM) is a multi-sectoral strategy and policy framework including industries, international organizations, government, academia and civil society, working to change how chemicals are used and produced so that their harmful effects on human health and the environment are minimized. SAICM recognizes the need to improve risk-reduction measures to prevent the adverse effects of chemicals on the health of vulnerable groups, such as children, pregnant women, fertile populations, the elderly, the poor and workers, as well as on susceptible environments.

As part of SAICM the third session of the International Conference on Chemicals Management in 2012 (ICCM3) agreed that EDCs met the criteria of an emerging policy issue. It adopted a resolution on EDCs stating that international cooperation to build awareness and understanding and promote actions on endocrine-disrupting chemicals as an emerging policy issue. The resolution further states that information dissemination and awareness-raising on EDCs are particularly relevant and that improving the availability of and access to information on such chemicals is a priority.

In 2012, UNEP and WHO, in collaboration with a working group of international experts, published the State of the Science of Endocrine Disrupting Chemicals - 2012 supporting the SAICM objective of information and knowledge sharing. The report identifies key concerns, novel data, and presents future needs. An accompanying summary is targeting decision makers in order to increase governments awareness on the EDCs issue. Overall, stakeholders agree on the need for further understanding and action on EDCs. At ICCM4 in 2015, stakeholders reconfirmed the need to address EDCs on a global level. Pursuing its goal of awareness raising, UNEP developed this brochure to reach policy makers and the general public and spread the conclusions of the UNEP-WHO 2012 report to reduce the environmental exposure to EDCs.

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Introduction

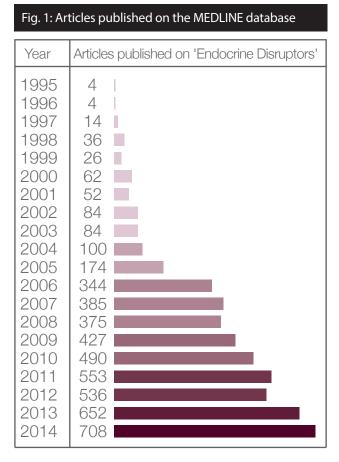


By promoting the sound management of chemicals throughout their life cycle, the UN Environment works to protect people and the environment from the harmful impacts of chemicals and hazardous waste.

In 1962, US scientist Rachel Carson published Silent Spring a critique and call to action on the impacts of pesticides on wildlife and the environment. Though heavily criticized at the time, the book launched a national debate over the role of science and policy makers' duty of care regarding new technologies. In countries around the world, similar debates have occurred as chemicals increasingly become part of everyday life – in the food we eat and the things we buy and use. As more studies have been conducted, the impacts of endocrine disrupting chemicals (EDCs) on humans and wildlife have come under greater scrutiny.

Concern About EDCs

People have been concerned about the impacts of EDCs for more than five decades, and scientists have increasingly sought to assess the impacts of EDCs on people and the environment. The MEDLINE database of life sciences research shows a great increase in the number of articles published on endocrine disruptors during the 20 years from 1995 to 2014.



01

EDCs Introduction

Milestones and Policy Action on EDCs

In the 1960's chemicals including DDT, PCBs and dioxins were early identified as hormone active substances. Below are examples of milestones and the policy actions drawn from different countries. The table illustrates developmental trends on EDCs and is not exhaustive.

1996 ●	
	US scientists Theo Colborn, Dianne Dumanoski and John Peterson Myers publish Our Stolen Future, bringing worldwide attention to scientific discoveries that some chemicals can interfere with hormonal action in humans and wildlife.
•	A landmark workshop in Weybridge, UK, on "The Impact of Endocrine Disruptors on Human Health and Wildlife" comes up with a commonly used definition of endocrine disruptors and calls for human studies on the effects of exposure to potential EDCs before and after birth.
1999 🔶	
	The European Commission adopted a 'Community Strategy for Endocrine Disruptors' aiming at increasing our understanding of endocrine disruption, making information available to the public, developing test methods to identify endocrine disruptors and beginning to address the risks arising from them.
2002	
	The World Health Organization (WHO) and the UN Environment Programme (UNEP) issue the first Global Assessment of the State-of-the-Science of Endocrine Disruptors, containing an agreed definition of EDCs (see p. 5 for the full definition).
2009 🔶	
	The Endocrine Society releases a peer-reviewed 'Scientific Statement' on the health effects of EDCs. The American Medical Association (AMA) adopts the statement and agrees to work with the US federal govern- ment to decrease public exposure to EDCs.
2012 🔶	
	The third session of the International Conference on Chemicals Management (ICCM3) in Nairobi, Kenya, agrees EDCs as an emerging policy issue. Member States resolve to support developing countries and countries with economies in transition to assess and reduce risks related to EDCs.
•	Argentina, Brazil and the US ban the use of bisphenol A (BPA) in baby bottles as a precautionary measure. BPA, a synthetic estrogen found in polycarbonate plastics, has been linked with reproductive and brain disorders, posing particular risk to young children. Ecuador, the EU and some European countries have already banned the use of BPA in similar products.
•	The Organization of Economic Cooperation and Development (OECD) releases its conceptual framework on EDCs. The OECD publishes a guidance document on standardized test guidelines for evaluating chemicals for endocrine disruption.
2013 🔶	
	WHO and UNEP issue State of the Science of Endocrine Disrupting Chemicals 2012, an update to the 2002 report.
•	Collegium Ramazzini, an international academy of scientists, releases its official position on EDCs and chemicals safety policy in the EU, calling for a precautionary approach that will protect people and workers.
•	At an EU conference on EDC policies in Brussels, Belgium, eighty-nine endocrine scientists sign the Berlaymont Declaration, expressing alarm over the increasing prevalence of endocrine-related diseases.
2015	
	The Journal of Clinical Endocrinology and Metabolism publishes a paper estimating that the burden of disease costs linked to EDC exposure in the EU is US\$175 billion.
	The Endocrine Society releases 2015 statements on EDC

The human endocrine system and EDCs



The endocrine system is made up of glands that produce hormones, which regulate many of life's essential activities, such as how we grow, reach sexual maturity and reproduce.

Endocrine glands release more than 100 chemicals into the bloodstream. Endocrine glands can be contrasted with exocrine glands that produce external secretions like saliva and sweat. The hormones released by the endocrine system act as chemical "messengers" that signal when and how to carry out certain physiological processes.

In humans for example, at the onset of puberty, the testes release male sex hormones (androgens) in boys, and the ovaries release female sex hormones (estrogens) in girls. These hormones prepare the body for reproductive functions and prompt the development of secondary sexual characteristics in young women and men.

Another set of activities relate to the thyroid hormones. Too much or too little thyroid activity

affects how the brain, heart, muscles, liver and other parts of the body work. It can affect how hot or cold someone usually feels, and whether they gain or lose weight easily.

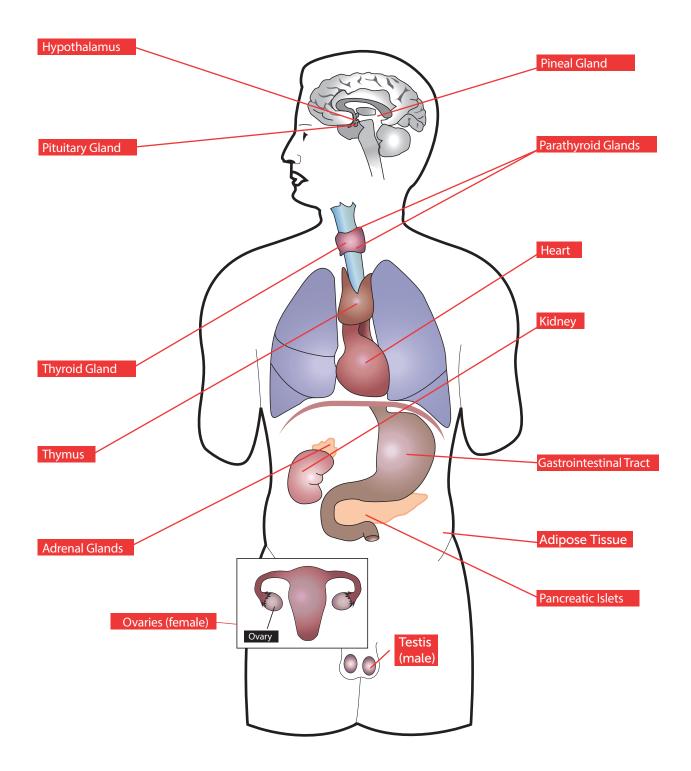
Hormones act on certain proteins in the body called receptors, which bind to specific hormones. This is often referred to as a lock-and-key mechanism the hormone is the "key" that "unlocks" the hormone receptor to do what is needed.

An example of this activity is when the pancreas releases insulin into the bloodstream as blood sugar rises after a meal. The insulin unlocks cells to allow sugar to be used for energy. It also helps the body to store surplus blood sugar in the liver, to be released as needed. Insulin resistance and Type 2 diabetes occur when this lock-and-key mechanism is damaged and the body becomes unable to use insulin properly.

EDCs The human endocrine system and EDCs

Fig. 2: The human endocrine system. Redrawn from fig. 1.1, WHO-UNEP State of the Science of Endocrine Disrupting Chemicals 2012.

UNEP diagram of human body with key parts marked, depicting major endocrine glands, i.e. pituitary, pineal, thyroid, parathyroid, hypothalamus, pancreas, adrenal, ovary (in women) and testis (in men).



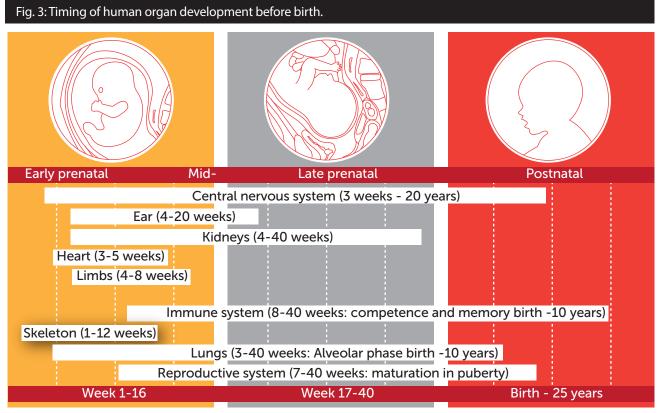
Hormone functions are essential to normal development, health and wellbeing. EDCs interfere with the body's normal processes in various ways. Some EDCs mimic the actions of the body's natural hormones; others may block or alter these actions. EDCs are able to interact with the body through the same pathways as the body's natural hormones.

The International Programme for Chemical Safety, a collaboration among three UN agencies – the World Health Organization, the International Labour Organization and the UN Environment Programme – agreed a definition of an endocrine disruptor, as **"...an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations."**

This is a challenge for assessing risks to human health and the environment.

Hormone action is mediated by receptors, and the relationship between the level of exposure to an EDC and its effects, may not be linear. Currently OECD has a guidance document on standardized test guidelines for evaluating chemicals for endocrine disruption. The traditional practice for assessing risk is to establish a safety threshold, below which there is no observable adverse effect, but this approach may not work for assessing risk from EDCs.

What has become clear over the years is that pregnant women and unborn children are at particular risk from exposure to EDCs during critical periods of development. A level of exposure that has little or no effect on adults can cause irreversible harm to unborn babies as their organs develop, (see fig. 3 to understand the vulnerable "windows" during pregnancy.) As hormones have a role in programming the body for functions that will take place later in life, EDCs can have an influence



Redrawn from fig. 1.4, WHO-UNEP State of the Science of Endocrine Disrupting Chemicals 2012.

that only becomes clear many years after exposure, or even in later generations.

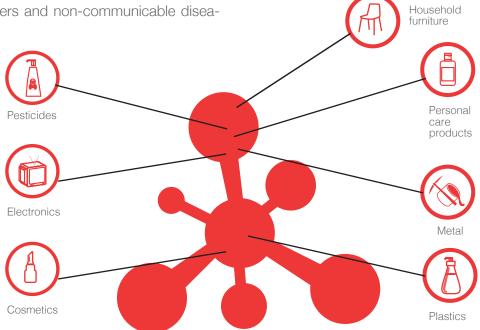
Most chemicals that have potential for endocrine disruption are manufactured, although some occur naturally. EDCs can be found in some common consumer products, including some plastics, metals, pesticides and personal care products such as soap and cosmetics. They can also be formed as breakdown products from chemicals that are released into the environment.

Studies have shown adverse outcomes in wildlife and laboratory animals exposed to EDCs, giving support to the concerns about human health impacts. This evidence is supported by human studies such as the case of the potent drug Diethylstilbestrol (DES).

The best-documented impacts of EDCs have been on reproductive functions. Some chemicals have been shown to disrupt development of male sex organs, via endocrine mechanisms. Other reproductive impacts that have been associated with EDC exposure including endometriosis and early puberty.

EDCs may also affect learning and memory, metabolism, immunity and even bone health. Scientists have linked these effects with various disorders and non-communicable diseases (NCDs), although this is still being debated.

The sharp rise in the incidence of some cancer since the 1940s may be related to the increased presence of EDCs in the environment, although the impact of aging and improved diagnosis on cancer incidence may need to be considered. Some EDCs may affect weight gain, insulin sensitivity and glucose tolerance, possibly playing a role in the increasing incidence of obesity around the world. Altered thyroid hormone action in pregnant women, due to insufficient iodine, autoimmune disease or EDC exposure, has been linked with cognitive and behavioral problems in their children, including reduced IQ, attention deficit hyperactivity disorder (ADHD) and autism.



EDCs in the environment



Chemicals are released into the environment through a wide range of human activities, including the use of pesticides in agriculture, various manufacturing processes, and the release of waste through burning, dumping and wastewater discharge. Some of these chemicals may include known endocrine disruptors that affect wildlife in different ways.

Fish and amphibians take up potential EDCs directly from contaminated wastewater via their external surfaces such as gills and skin. Contaminated soil and sediments can affect the worms, snails and insects eaten by birds and fish. Fish-eating mammals, such as otters, may be particularly vulnerable to EDCs since chemicals that they absorb can accumulate in the fish tissue and increase in concentration at the top of the food chain, and they tend to live in rivers and lakes close to farmlands and industrial sites. Birds and reptiles may be affected as their egg composition can contain contaminants that embryos are exposed to while they develop.

Specific wildlife populations have been able to recover when potential EDCs were eliminated or greatly reduced in the environment.

For 40 years, the chemical tributyltin was used as a biocide in anti-fouling paint, applied to boat hulls to discourage the growth of barnacles.

EDCs and fathead minnow in Canada

A seven-year study of a freshwater fish, fathead minnow, in northwestern Ontario, Canada, showed that exposure to wastewater containing low levels of estrogen resulted in feminization of male fish. Male fish downstream of wastewater release sites produced vitellogenin, an egg protein, and early-stage eggs in their testes. Egg development in female fishes was also affected.

Eventually researchers attributed this phenomenon to the presence of various natural and synthetic estrogens in the wastewater, including components of birth-control pills and nonylphenols, which are found in laundry detergents and other household and industrial products.

Eventually, fathead minnow almost faced extinction, showing that chronic exposure to EDCs, even at low levels, can potentially wipe out wild fish populations.

The paint was formulated to release the biocide slowly into the environment.

Studies of sea snails in some of the harbors and marinas that were contaminated with tributyltin found that female sea snails in those areas had begun to grow male sex organs, a condition known as imposex. The condition eventually led to the collapse of the mollusk population in some areas.

Only after the use of tributyltin was restricted for the use of small boats, from the late1980s and early 1990s, did mollusk populations begin to recover in some areas. A global ban came into force in 2008 on the use of tributyltin for all shipping.

Similarly, European otter populations, which declined between the 1960s and 1980s, began to recover in Sweden in the 1990s as the occurrence of a class of chemicals called poly-

EDCs EDCs in the environment

chlorinated biphenyls (PCBs) decreased in the Swedish environment. Their recovery supported the idea that PCB contamination had been the main cause of decline. Similar recovery occurred in Baltic gray seal populations, implicating PCBs as a leading cause of reproductive problems, among other factors contributing to population decline.

PCBs and other persistent organic pollutants (POPs), so named because they remain and accumulate in the environment and hence affect the environment for a long time, have been earmarked for elimination under the Stockholm Convention on POPs. Some POPs are thought to be EDCs, including PCBs and polybrominated diphenly ethers (PBDEs). PCBs are still found in many areas of the world in transformer oil used in transformers used to transfer electricity.

While some potential EDCs are rapidly transformed by sunlight, bacteria and chemical processes in the environment, others can remain in the environment for months and years (see Fig. 4). Some modest decreases in PCBs and PBDEs have been recorded, but these chemicals persist in the environment and wildlife for long periods and they are causing adverse effects in different ways.

Some chemicals have low solubility in water and are stored in the fatty tissues of predatory animals. Older and larger animals have been found to have higher concentrations of such chemicals, which remain in their bodies throughout their lifespans.

Fate and transport in the environment: Air and ocean currents can transmit chemicals far from their source. Chemicals can also be naturally transported globally, in which chemicals evaporate into the atmosphere. As air currents move towards colder climates, condensation takes place, re-depositing the same chemicals on land and sea. The long-range transport that takes place in this way means that some EDCs have affected Arctic people and sea life many miles away from factories, farms and other release sites (see Fig.4).

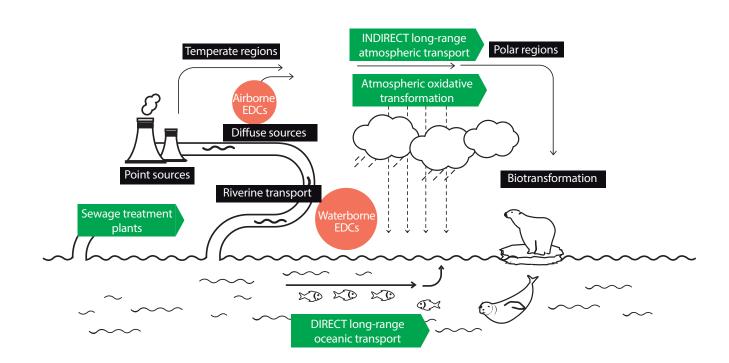


Fig. 4: How chemicals travel in the environment.

EDCs and human health



People can be exposed to EDCs and potential EDCs through food, water, dust, air and skin contact with various materials. EDCs may be found among the chemical additives in electronics and electrical equipment, household cleaning products, textiles and furniture.

Children have a higher metabolic rate than adults and less fatty tissue to absorb substances, so what they ingest has a greater impact on their bodies. They may touch, handle or suck on furniture, bedding and toys: this hand-to-mouth activity can mean they are also more exposed to certain chemicals in the home. Concentrations of certain chemicals being evaluated as potential EDCs, used in common household items, have been found to be much higher in indoor than outdoor environments.

Some jobs expose workers to high levels of EDCs. For example, blood tests of operators involved in spraying DDT, which is still used as a lifesaving method in areas where malaria and other diseases are prevalent, showed they had much higher concentrations of the chemical in their blood, compared with people whose homes were not sprayed. Farm workers involved in harvesting or processing crops may come in contact with pesticides, some of which may be potential endocrine disruptors. Wokers who handle or recycle electronic waste products may also be exposed to high levels of potential EDCs.

Other sources of exposure to EDCs or potential EDCs are from thermal paper used for cash register receipts and the lining of some food containers, both of which contain bisphenol A (BPA). Contact with chemicals used in cosmetics and personal care products also result in exposure to EDCs or potential EDCs.

Polycyclic aromatic hydrocarbons (PAHs) emitted from wood and coal burning, are an airborne source of potential EDCs. In low income countries and rural areas where these fuels are frequently used for cooking and heating, people may also be exposed to PAHs.

Heavy metals, including lead and mercury are thought to be potential EDCs, and also affect the brain and nervous system. Other heavy metals like cadmium and arsenic are also potential EDCs. Groundwater, including water from wells and pumps, may be contaminated with arsenic in some places, notably Bangladesh, India and near mining sites in other countries. Consumption of predatory fish and mammals, in some locations, heightens the risk of mercury exposure. Pregnant women and women who might become pregnant, nursing mothers and young children are particularly at risk. Fish and shellfish are important in a healthy diet, so it's best to seek local guidance, where available, about the safety of fish caught in local rivers and lakes.

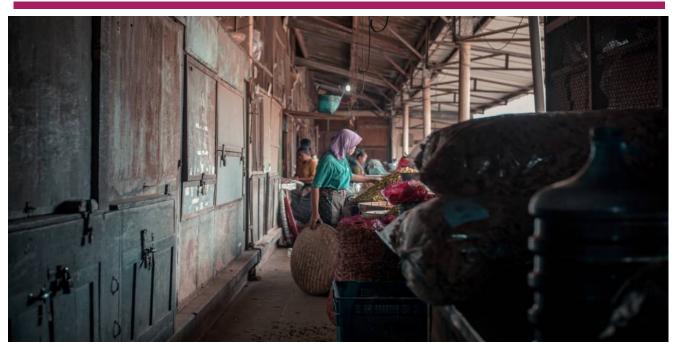
Even though exposure to specific EDCs may be low, there can be a "cocktail effect" as various EDCs combine or interact to affect the way our bodies work. Researchers have noted that most current knowledge about the chemical action of endocrine disruptors comes from information about responses to single types of EDCs, whereas in reality, people are exposed to low levels of many different potential EDCs over long periods. They warn that the cocktail effect could be responsible for exacerbating the adverse effects of certain chemicals

Scientists have tried to quantify the economic cost of the health impacts of EDCs.

In the EU, a 2015 study considered the cost of exposure to various potential EDCs. Neurodevelopment experts involved in the study estimated that prenatal exposure to organophosphate pesticides is linked with 59,300 cases of intellectual disability annually in Europe, as well as reducing IQ levels and contributing to new cases of autism and ADHD. Experts on male infertility considered that exposure to phthalates (a group of chemicals used to soften and increase the flexibility of plastic and vinyl), is contributing to greater demand for assisted reproductive technology procedures from couples wishing to conceive. A panel on obesity and diabetes identified exposure to phthalates as a factor in obesity and diabetes in older women, while prenatal exposure to BPA was linked with 42,400 new cases of childhood obesity annually.

In total, the study estimated that the annual economic burden of these impacts at around \$165 billion (€157 billion) in the EU.

Steps to reduce exposure



People are exposed to EDCs and potential EDCs in daily life in four main ways:

Crops we grow

Things we make



Farm workers as well as consumers are vulnerable to the impacts of many different kinds of pesticides, some of which are EDCs.



Manufacturing and recycling activities involve a wide array of chemicals that may include EDCs.

Places we work and live



Our homes, factories and offices expose workers to EDCs in electronic and electrical equipment, building materials and textiles.

Things we buy



Many household items, including clothing, bedding, personal care products and plastic containers contain potential EDCs such as phthalates, perfluorochemicals and phenols.

Some countries have begun taking steps to reduce exposure to EDCs and potential EDCs. 'Nordic Swan,' for example, is an eco-label that assures consumers of environmental quality through a system of independent testing and certification. In Italy, the government has promoted the 'Italian Decalogue,' a handbook that explains the potential health risks from EDCs in common household products.

While chemicals provide many benefits in everyday life, babies in the womb and young children are at important developmental stages. As far as possible, they should be protected from the potential adverse impacts of chemicals.

Moving forward in the face of uncertainty



The prevalence of chemicals in the environment is a big challenge for current management regimes. For EDCs and potential EDCs that are listed in the Stockholm Convention, there are national actions to prohibit production, use, import and export.

Consumers around the world need information to enable choices, but this is often not available. A 2012 study found labeling of many products, including air fresheners, sunscreen and cosmetics, to be incomplete, with many chemicals not being listed.

Workers in developing countries, particularly those in the informal sector, such as waste pickers, are at high risk – for example, when recycling electronic waste through open burning and acid baths that release toxic chemicals. In many countries, it is migrant workers, women, children and the poor who are most exposed to hazardous waste in their daily work. Even though most chemicals are produced and used in the developed world, at the current growth rates, developing countries by the year 2020 will be producing 31% of all manufactured chemicals, and using 33%. The time is right for increased cooperation and action. There may never be full certainty about the impacts of EDCs, but we can take a precautionary approach to the use of chemicals, through a holistic approach that considers all aspects of chemicals production, use, storage and disposal. We can also phase in less harmful substitutes.

The role of each Sector



Governments can establish clear and consistent laws and regulatory measures on agricultural, industrial processes, building regulations, consumer products and enforce regulation that are adopted. They can prohibit production and use of certain substances and/or require appropriate labeling and disclosure of information about chemical components of products and industrial processes. Governments can also continue to provide training to regulatory authorities and small and medium enterprises (SMEs) for sound chemicals management, and work with industry actors that are leaders in sound chemicals management.



Civil society organizations have been leaders in identifying issues of concern for government and industry action. They can continue to make information about EDCs widely available, promote thoughtful consumption, and identify at-risk groups for special attention.



Industry can consider non-chemical or less harmful alternatives when developing products. In particular, they should disclose information that will enable sound chemicals management, and work with governments to establish strong industry standards and have safe workplaces.



International organizations, such as the UN Environment, bring together countries and can help provide access to reliable and balanced information, build capacity, and promote action for the sound management of chemicals. They can continue to research and share information with countries, industry and civil society organizations. They can also provide information on best practices for management.



Further resources and contact information

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Website of the Strategic Approach to International Chemicals Management (SAICM): http://www.saicm.org Adopted by the International Conference on Chemicals Management (ICCM) on 6 February 2006 in Dubai, United Arab Emirates, SAICM is an policy framework to foster the sound management of chemicals, supported by UN Member States.

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