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Introduction

1.1 Chemistry and Development

World War II was one of the most destructive periods of modern history for humanity, but also one of the most inventive periods for the design and production of new chemicals. It was an epoch of such unprecedented innovation that this period has been often referred to as a second chemical revolution. That golden age for chemistry has had, for better or for worse, an undeniable influence in our lives and in the development of civilization. Food production, medicine, pharmacology, and defense underwent unprecedented expansion during those years of scientific and technological advances, and these developments are profoundly influential even today. Regardless of the origin and the underlying reasons for such scientific progress, this historical era supported the development of new chemicals and materials that have improved human welfare in terms of health, longevity, and general living conditions both at the global as well as individual scale. This, however, has also imposed an underestimated burden.

During the first half of the twentieth century, the continuous expansion of the chemical industry and the use of chemicals in many aspects of our life contributed toward creating a positive image of chemistry in our society. Things changed, however, during the 1960s, when two widely sold books began to generate a different kind of social awareness of chemistry and chemical compounds. *Silent Spring* [1], focused on the undesirable effects of the indiscriminate use of pesticides on the environment and *Our Stolen Future* [2] sought to explain how certain chemicals interact with hormones in humans and wildlife. These two works succeeded in providing a new perspective of chemistry among the populace. The ideas presented in these books, together with information on a series of environmental disasters over the following decades, caused by bad practices in the use and handling of chemicals in certain chemical industries and also by unsafe factory design, cast a dark shadow over everything related to chemistry and chemicals. Examples of severe episodes of pollution are the Seveso (Italy) disaster caused by the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) leak in 1976, the Love Canal evacuations in Niagara (New York) caused by the spill of 21,000 t of toxic waste that was buried underground by a local company from the 1940s until 1978,

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and the Union Carbide leak in Bhopal (India) in 1984, when around half a million people were exposed to methyl isocyanate gas and other substances, and many of them died, which is considered the worst disaster in the chemical industry ever.

All these contributed to an enormous loss of prestige and increased societal concerns about anything related to chemistry throughout the second part of the twentieth century. Despite the many benefits that chemistry has provided for our lives, not to mention that chemistry itself is at the origin of life and existence, the words “chemistry” or “chemical” has taken on a negative connotation in recent times.

Things have begun to change back again in recent decades. Our awareness of the need to preserve the environment for generations to come has risen greatly in the last few years, and is reflected in public opinion, international organizations, governments and, of course, chemists. Profuse legislation has been issued worldwide to set the acceptable levels of pollutants in water, air, or soil, while strong control mechanisms have been implemented to protect the environment and human health. More specific to the chemical industry, numerous documents and institutional publications indicate increasing concerns about bad practices that are prevalent in the production and use of hazardous chemicals. In 1988, the United Nations Environment Programme prompted the signing of the “International declaration on a cleaner production,” which remains applicable today. In this programme, a comprehensive preventive strategy was developed to describe processes, products, and services in the interest of health and safety as well as social and environmental welfare. Concepts such as eco-efficiency, ecological productivity, and pollution prevention were introduced at that time to establish the practices that we apply today. Also, new contributions arising from industry, driven by the World Business Council for Sustainable Development, are remarkable. This international organization formed by more than 125 large companies in 35 countries, and 20 related industries is grouped around three concepts: economic growth, ecological balance, and social development; it has become a forum since 1990, which promotes sustainable development in the world industry.

In 1990, the USEPA, through a document called the Pollution Prevention Act, which establishes US policies to “prevent or reduce pollution on any occasion possible,” an office within the Environmental Protection Agency (EPA), Office for Pollution Prevention and Toxics (OPPT), has promoted the preparation and production of new chemicals that are less hazardous to human health and the environment. The goal set is to replace dangerous substances used in industry as well as to improve existing methods of production, to minimize environmental impact. On this basis, a specific project called Design for the Environment, to address “alternative synthetic pathways for pollution prevention,” has been developed. This program is actually considered the seed of Green Chemistry. Simultaneously, the Clinton administration launched the “Presidential Green Chemistry Challenge” together with the EPA’s design for the environment and the scientific community. Since 1996, five annual prizes are awarded focusing on the following priority areas of chemistry: alternative synthetic pathways and reaction conditions and the design of safer chemicals. This contest has helped to improve more sustainable methods and procedures in chemistry, especially for industry, to synthesize safer chemicals and to gain a deeper understanding and complete knowledge of the impact of synthetic compounds on the environment. It is now clear that the uses and the benefits of chemicals, either known or new, must be accompanied by extensive investigation of possible hazards these chemicals may present, as well as an evaluation of the environmental risks related to their production, transport, and handling, and the implementation of an efficient communication policy.

The chemical industry plays an essential role in today's economy in developed countries, being considered a strategic sector, and contributing significantly to the gross domestic product. For example, the chemical industry is the largest manufacturing sector in the United States and the second largest in Europe and Japan, accounting for approximately 5% of the gross domestic product in each of these countries. This represents more than $1.6 trillion of the total market and has provided employment to over 10 million people globally.

1.2 Pollution and Contamination

Pollution is the process of dirtying land, water, air, or other parts of the environment, or making them inappropriate places for use. The process is complex, driven by the introduction of undesirable substances, pathogens, or energy that disturbs both the environment's natural status and the development of specific areas. There are three main groups that contribute to pollution, namely: chemical, physical, and microbiological. Sometimes, the term "contamination" is used as well. Although in most cases, this can be considered a synonym, confusion may arise because of elusive differences of degree. In 2007, Chapman [3] proposed a clarification in this regard:

> *Contamination is simply the presence of a substance where it should not be or at concentrations above background. Pollution is contamination that results in, or can result in, adverse biological effects to resident communities. All pollutants are contaminants, but not all contaminants are pollutants.*

On the other hand, "emissions" is the term used to describe contaminants that are released into the environment or emitted by various sources. There are many sources of emissions: natural and anthropogenic.

Natural sources include biogenic emissions that are caused by living organisms and interaction of water bodies or the atmosphere with soil, rocks, or sediments. During the course of the earth's history, the composition and the average of the compounds present in the diverse spheres have been changing either by natural procedures or by human activities. Accepted data comparing emissions of gases of natural and human origin are listed in Table 1.1

Sources of contamination from human activities (anthropogenic) are diverse. They include emissions from sources such as transport, industry and factories, agriculture livestock, or household activities.

Table 1.1 Example of emissions of natural and human origin.[a)]

Emission	Natural (million t yr^{-1})	Human (million t yr^{-1})	Emission	Natural (million t yr^{-1})	Human (million t yr^{-1})
CO_2	600,000	22,000	NH_3	1200	7
CO	3800	550	NO_2	770	53
Hydrocarbons	2600	90	N_2O	145	4
CH_4	1600	110	SO_2	20	150

a) Data taken from Ref. [4].

1.3 Chemical Pollutants

Chemical pollutants are organic or inorganic compounds that can harm the environment. They can be substances that are directly emitted to the environment by different means or substances resulting from chemical or photochemical reactions or metabolic transformations by living organisms. The reactions give rise to primary pollutants, while transformations produce secondary pollutants. The latter are usually more difficult to handle, especially when emitted after being metabolized by a living organism from a former toxic or potentially toxic substance, in which case both the original molecule and the metabolite are considered pollutants.

The number of described organic and inorganic substances to date exceeds 127 million[1] and most are organic compounds. Therefore, it follows that most pollutants are organic molecules. From the environmental chemistry point of view, organic pollutants can be classified as volatile organic compounds (VOCs) and persistent organic pollutants (POPs).

VOCs are molecules with a low number of carbons in their structures (no more than 10 or 12) that have low boiling points, and vapor-pressure values, usually. Therefore, they evaporate readily and their main occurrence is in the atmosphere, but they can also be found in surface waters, ground waters, or soils. Typical examples of such compounds are common organic solvents, such as trihalomethanes or formaldehyde.

POPs are either semi-volatile molecules or molecules with a low volatility that have remarkable toxicity. POPs strongly resist chemical and biological degradation, so they may have a half-life of years or decades in soils or waters and several days in the atmosphere. But there is no consensus on how long the half-life should be in a given media for a compound to be considered "persistent" [5].

Between aquatic media and soils, POPs partition preferably to solids, mainly on soil organic matter, avoiding the aqueous phase and also partition into lipids in living organisms rather than remaining in the aqueous milieu of cells; thus, they may be stored in fatty tissue. This is a consequence of being typically "water-hating" and "fat-loving" because of their hydrophobicity and liposolubility and therefore they are bioaccumulative. On the other hand, they may

1 Data taken from the Chemical Abstracts Service (February 21, 2017), http://www.cas.org.

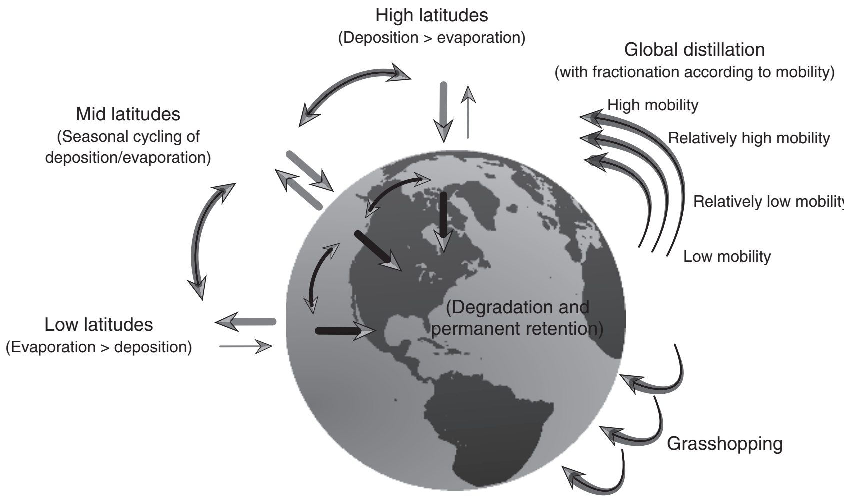

Figure 1.1 POP global migration processes. (Data taken from Ref. [6].)

volatilize partially from soils, vegetation, and water bodies into the atmosphere. This feature, together with their resistance to degradation reactions in air enables them to travel great distances by a mechanism known as global distillation or grasshopper effect, causing a pollutant "jump," and re-deposit several times from the Ecuador to colder areas. As a result, POPs are able to accumulate in areas far from where they were used or emitted (see Figure 1.1).

Included in this group of POPs are pesticides such as 1,1,1-trichloro-2,2-bis (*p*-chlorophenyl)ethane (DDT) and their metabolites, chlorinated pesticides such as aldrin, toxaphene, other chlorinated molecules such as hexachlorobenzene, polychlorinated biphenyls, and by-products formed in the fabrication of many other chemicals, or in the combustion of fuels or wastes such as dioxins and dibenzofurans. Many POPs are included in the Stockholm convention and are no longer produced or strongly regulated.

According to USEPA, pollutants can be classified into two groups:

- Priority pollutants.
- Emerging pollutants.

EPA's priority pollutants are a set of regulated chemical substances that have been selected on the basis of their known or suspected carcinogenicity, mutagenicity, teratogenicity, or high acute toxicity, and for which there are well-defined analytical test methods. They have been established in the Clean Water Act (CWA), as a basic structure for regulating discharges of pollutants into US waters, as well as regulating quality standards for surface waters. CWA, first enacted in 1948, was later called the "Federal Water Pollution Control Act." In 1972, the act was significantly reorganized and expanded to become the currently known CWA.[2]

2 Summary of the Clean Water Act. Accessed April 26, 2017. http://www2.epa.gov/laws-regulations/summary-clean-water-act.

Most of these priority pollutants are subject to regulation by rules and laws of individual countries or supranational agencies. This group includes substances such as POP, heavy metals, some pesticides, or polycyclic aromatic hydrocarbons (PAHs). Within this priority category, substances or groups of substances are well known to be toxic, bio-accumulative, and hazardous for the environment. In the European Union (EU), the levels of organic priority pollutants in waters, including some metals (Cd, Ni, Hg, and Pb), are regulated according to the Directive 2008/105/EC [7]. For the United States, the EPA in the CWA references, the list of toxic pollutants includes a set of 126 priority pollutants.

1.4 Pollutants in the Environment

According to the World Health Organization (WHO), more than 100,000 chemicals are released into the global environment every year as a consequence of their production, use, and disposal. The fate of a chemical substance depends on its chemical structure and physicochemical properties, in combination with the characteristics of the environment where it is released.

Pollutants discharged into the environment may be "natural" or "human-made." A "natural" pollutant is a substance that can appear without human introduction. For example, trace metals can be considered naturally occurring substances and are generally found in the environment only in moderate amounts that do not pose health threats. However, natural pollutants can also have anthropogenic origins. Human activities often cause the release of a large amount of inorganic compounds containing metals into the environment and it is not the mere presence of a contaminant that makes it toxic, but its concentration.

The stability, transport, and transformation of chemical compounds in the environment are consequences of several factors. Some of them depend on the intrinsic nature of the compound, such as chemical stability, vapor pressure, or solubility in water, while others depend on environmental conditions, such as partition-coefficient octanol/water and air/water sorption processes in soils, or bioconcentration. Chemical compounds in the environment can be transformed by chemical, photochemical, or microbiological processes or by a combination of these. The main reactions of chemical compounds in the environment are the following:

- Hydrolysis.
- Acid–base transformations.
- Redox reactions.
- Substitution.
- Elimination.
- Complexation.
- Precipitation.

Metal derivatives undergo chemical transformations that, for example, alter toxicity depending on oxidation state, but they stay in the environment unaltered. However, organic compounds can be transformed or not, depending on the structure. In many cases, a combination of individual processes takes place, giving rise to simpler molecules that can be degraded by microorganisms. Moreover, other chemical compounds are resistant to degradation and remain almost unchanged in the environment. These are called POPs and can be found in soil, water bodies, and living organisms tissues, because of their bioaccumulation. Smaller organic molecules have a high tendency to be present in the atmosphere because of their high vapor-pressure values, VOCs, but they can also be found in water bodies, absorbed in soil particles or in plants that can be ingested by animals or humans.

1.5 Concept of Emerging Pollutants

Emerging pollutants (EPs) are chemical substances, commonly not regulated, which can be detected in low or very low concentrations by analytical techniques, raising special concern because their long-term adverse effects on the environment and on human health remain unknown. EPs can be defined as compounds of different origin and chemical nature whose presence in the environment, or by consequences of their presence, have gone largely unnoticed and remain unregulated.

International organizations and national agencies of specific countries have developed some definitions of EPs, which illustrate different aspects related to the issue and which can help to understand the dimension of the problem and its consequences.

The network of reference laboratories, research centers, and related organizations for monitoring emerging environmental substances in Europe (NORMAN) is an international project[3] funded in 2005 by the European Commission in order to promote the creation of a permanent network among reference laboratories and research centers, in collaboration with the parties involved (industry, standardization bodies, non-governmental organizations, etc.) [8].

According to EU NORMAN network such chemicals are:

> Substances that have been detected in the environment, but which are currently not included in routine monitoring programs at the EU level and whose fate, behavior, and (eco)toxicological effects are not well understood. In the United States, the EPA has replaced the expression "EPs" with the abbreviation CEC.[4] NORMAN has identified a list of the chemicals most frequently considered as emerging substances and EPs.[5] The substances are selected by a workshop (NORMAN Prioritisation Working Group), based on current citations in the scientific literature, and included in the definition of "emerging substances" and "EPs" given in the NORMAN glossary of terms, which are regularly revised.

3 Network of reference laboratories, research centers and related organizations for monitoring of emerging environmental substances. Accessed February 21, 2017. http://www.norman-network.net.
4 Contaminants of Emerging Concern including Pharmaceuticals and Personal Care Products. Accessed April 26, 2017. http://water.epa.gov/scitech/cec.
5 (List of Emerging Substances latest update February 2016), http://www.norman-network.net/?q=node/19.

According to the U.S. Geological Survey (USGS), CECs are defined as:

> *Any synthetic or naturally occurring chemical or any microorganism that is not commonly monitored in the environment but has the potential to enter the environment and cause known or suspected adverse ecological and/or human health effects* [9].

A representative example of this item can be found in some cases of emerging chemical or microbial contaminants to the environment, which have likely occurred for a long time but have not been recognized for years until the development of new analytic methods.

Because of the presence of CECs in low concentrations, some members of the scientific community have coined the term “micro-pollutants.” These chemical compounds of emerging concern are present in wastewater, soil, ground water, or drinking water in low to very low concentrations (pg L^{-1} to ng L^{-1}) [10].

A remarkable feature of EPs is their continuous production and consumption, and consequently continuous introduction into the environment. Due to the continuous exposure they need not be persistent to cause adverse long-term effects.

According to this, EPs may be new substances, or on the contrary, they may have been long present in the environment but only recently detected. We may just be beginning to understand their effect on the environment or human health, or we may only now have the ability to detect them in the environment [9].

In summary, further research and tests are required. EPs are prospects to be included in regulatory rules for an appropriate control and prevention of pollution.

1.6 Historical Background of Emerging Pollutants

Concern on EP motivates the development of analytical techniques in order to detect chemical compounds in a μg and even pg range of concentrations, especially in water samples. For example, in 2002 USGS published a study that detected the presence of pharmaceuticals, hormones, and other organic compounds in streams all over the United States down to trace levels. This agency considered five new analytical methods by that time, which detected concentrations of 95 organic substances in surface water from samples taken between 1999 and 2000 from 139 streams across 30 US states. Samples showed detectable quantities of organic wastewater contaminants and 82 of the 95 target compounds were found [11].

The study constantly being brought up to date in order to control the measurement of 263 compounds, can be consulted online for different matrices.[6] The main results of this study can be extrapolated to other areas. According to NORMAN, at least 700 substances, including some metabolites of such substances,

6 USGS: Contaminants of Emerging Concern in the Environment. Accessed April 23, 2017. http://toxics.usgs.gov/investigations/cec/index.php. An exhaustive list of published emerging contaminants and the common analytical methods used for determining EPs is also available.

are categorized into several classes, which have been identified in the European aquatic environment [12].

From all the above discussions, EPs may be potentially considered in the next few years as priority substances and subject to regulation. Most of these new pollutants are caused by human activity over the last few decades. They come from several branches of industry and scientific research and are related to lifestyle habits, while some are relatively new, such as a variety of chemicals coming from the appearance of new materials or related to nanotechnology. In other cases, daily household activities have made some household chemicals or pharmaceutical products appear in a massive way. Additionally, feed-production methods use antibiotics, antiseptics, or plaguicides as common products used in the prevention of diseases and elimination of pests in livestock and crops [13].

In some cases, the release of an emerging chemical or microbial contaminant into the environment has likely occurred for a long time but may not have been recognized until the development of new detection methods. In other cases, the synthesis of new chemicals or changes in the use and disposal of existing chemicals can create new sources of emerging contaminants. In other words, CECs are substances that we are beginning to suspect could cause harm. They may be new substances or may have been long used but have only been recently found in the environment. We may just be beginning to understand their effect on the environment and on human health, or we may only now have the ability to detect them in the environment [9].

1.7 Classification of Emerging Pollutants

EPs can be classified in several ways based on their origin, use, potential effects, or environmental fate. Some major groups considered as EPs are summarized as follows:

- Pharmaceutical and veterinary products.
- Disinfectants and biocides.
- Illicit drugs.
- Personal care chemicals and other lifestyle products.
- Industrial chemicals.
- Food additives.
- Water disinfection by-products.
- Nanomaterials.
- Waterborne pathogens.
- Biological toxins.

Other categories describe their nature, such as surfactants that can be used in detergents to aid grease removal and in cosmetics as an emulsifier; or synthetic hormones that mimic the action of natural hormones. Unfortunately, these categories can overlap, leading to some confusion, and there is no standardized set of categories used in the various studies on CECs. Some of the most common terms used to categorize CECs are listed in Table 1.2.

Table 1.2 Representative list of EPs.

Category	Compounds
Veterinary and human antibiotics	Trimethoprim, erythromycin, lincomycin, sulfamethoxazole, ampicillin, azithromycin, doxycycline, amoxicillin
Analgetics, anti-inflammatory drugs	Codeine, ibuprofen, acetaminophen, aspirin, diclofenac, fenoprofen, dipyrone metabolites
Psychiatric drugs	Diazepam, carbamazepine, lorazepam, bromazepam
Lipid regulators	Bezafibrate, clofibric acid, fenofibric acid, atorvastatin, amlodipine, cilazapril, simvastatin, enalapril
β-Blockers	Metoprolol, propranolol, timolol, bisoprolol
X-ray contrast agents	Iopromide, iothalamic acid, diatrizoic acid,
Steroids & hormones	Estradiol, estrone, estriol, diethylstilbestrol,
Drugs of abuse	Morphine, dihydrocodeine, cocaine
Sun-screen agents, insect repellents	Benzophenone, 3-(4-methylbenzylidene)camphor, *N,N*-diethyl-3-methyl-benz-amide
Fragrances	Nitro, polycyclic, and macrocyclic musks
Biocides	Triclosan, 2-benzyl-4-chlorophenol
Detergents	2-[2-(4-Nonylphenoxy)ethoxy]ethanol, 2-[2-(4-octylphenoxy)ethoxy]ethanol
Food additives	Sucralose, triacetin
Antioxidants	2,6-Di-*tert*-butylphenol
Water (disinfection)	2,2,2-Trichloroacetamide, chloroacetaldehyde
Gasoline additives	*tert*-Butyl methyl ether, dialkyl ethers
Anticorrosives	1*H*-Benzotriazole,
Antifoaming agents	2,4,7,9-Tetramethyl-5-decyne-4,7-diol
Antifouling compounds	Organotins (dibutyltin and triphenyltin ions), cybutryne
Plasticisers	Bisphenol A
Wood preservatives	2,4-Dinitrophenol
Flame retardants and impurities	Polybrominated diphenyl ethers (PBDEs), tetrabromobisphenol A, C_{10}–C_{13} polychlorinated alkanes, tris(2-chloroethyl) phosphate, polybromonated biphenyls (PBBs), polybromonated dibenzo-*p*-dioxins (PBDDs), polybromonated dibenzofurans (PBDFs), hexabromocyclododecanes (HBCDs)
Perfluorinated compounds	Perfluoroctane sulfonates (PFOS), perfluoroctanoic acid
Siloxanes	Cyclic (hexamethylcyclotrisiloxane, octamethylcyclotetrasiloxane, decamethylcyclopentasiloxane,); linear (octamethyltrisiloxane, decamethyltetrasiloxane, dodecamethylpentasiloxane,)
Algal toxins	Microcystins (microcystin-LR)
Bio-terrorism/sabotage agents	Chloropicrin
Nanoparticles	Limestone (nanoparticles), titanium dioxide (nanoparticles)
Pesticides	Organophosphorus pesticides, thiocarbamates, 2-aminobenzimidazole

1.8 Regulations and Normatives

EPs are by definition compounds that are not subject to regulation. Regulations and controls are focused on traditional pollutants, and different organizations and governmental institutions around the world have normatives and directives to preserve environmental quality, especially related to waters, whether surface or underground waters, which may be potentially used for human consumption. On the other hand, such institutions periodically present rules on different aspects of emerging contaminants (e.g. WHO, food and agriculture organization of the United Nations (FAO), joint FAO/WHO expert committee on food additives (JECFA), USGS, USEPA, Australasian society for ecotoxicology (SETAC-AU), etc.), all paying attention to the substances of special concern because of their potential adverse effects. Therefore, it is possible to find legislation and recommendations at several levels, according to the tested or potential effects of chemical substances.

The European Commission [7] has outlined a legislation covering a broad range of organic and inorganic pollutants over the years. However, the legislation is expected to broaden to encompass a greater number of municipally derived chemicals described as CECs. For example, following the recent proposal, pharmaceuticals 17β-estradiol (E2), 17α-ethynylestradiol (EE2), and diclofenac have been designated as priority hazardous substance. Proposed legislative targets for consent were 0.4, 0.035, and 100 ng L^{-1} for E2, EE2, and diclofenac, respectively [14].

The EPA identifies contaminants to regulate the drinking water in the United States, and has outlined three levels of EPA-set regulatory limits for the amounts of certain contaminants in water provided by the public-water systems. These contaminant standards are required by the Safe Drinking Water Act (SDWA). The EPA seeks to protect public health by implementing the SDWA provisions while working with governments, agencies, tribes, and many other partners.

The National Primary Drinking Water Regulations (NPDWRs) comprise a set of mandatory water quality standards for drinking-water contaminants based on the concept of "maximum contaminant levels" (MCLs) to protect the population against substances that present a risk to human health. Primary standards and treatment techniques for these substances limit the levels of contaminants in drinking water, such as microorganisms, disinfectants, and a group of inorganic and organic chemicals, including radionuclides.

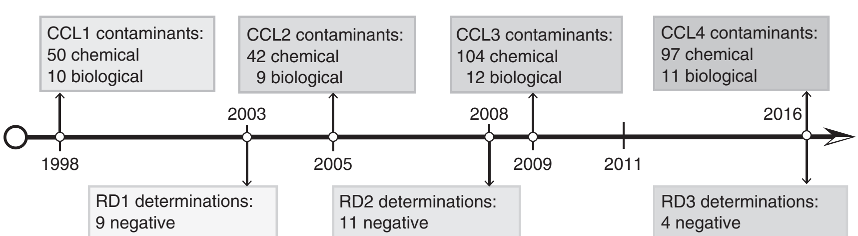

Figure 1.2 Timeline of EPA regulations and lists of contaminants.

Table 1.3 Toxicological guideline values established by EFSA and JECFA.[a),b)]

Element/species	Year [Reference]	Type	Value
Metals			
Mercury	2011 [15]	PTWI	4 μg kg^{-1} (bw $week^{-1}$)
	2012 [16]	TWI	4 μg kg^{-1} (bw $week^{-1}$)
Methylmercury	2003 [17]	PTWI	1.6 μg kg^{-1} (bw $week^{-1}$)
	2012 [16]	TWI	1.3 μg kg^{-1} (bw $week^{-1}$)
Lead	2011 [18]	BMDL01	0.50 μg kg^{-1} (bw day^{-1})
Cadmium	2011 [18]	PTMI	25 μg kg^{-1} (bw $month^{-1}$)
	2009 [19]	TWI	2.5 μg kg^{-1} (bw $week^{-1}$)
Arsenic	2011 [15]	BMDL0.5	2–7 μg kg^{-1} (bw d^{-1})
	2009 [20]	BMDL10	0.3–8 μg kg^{-1} (bw d^{-1})
Pharmaceuticals and personal care products			
Benzylpenicillin	1990 [21]	ADI	<30 μg kg^{-1} bw
Oxytetracycline	2002 [22]	ADI	0–30 μg kg^{-1} bw
Emamectin	2013 [23]	ADI	0–0.5 μg kg^{-1} bw
Derquantel	2012 [24]	ADI	0–0.3 μg kg^{-1} bw
Flumequine	2007 [25]	ADI	0–30 μg kg^{-1} bw
Carazolol	1995 [26]	ADI	0–0.1 μg kg^{-1} bw
Dexamethasone	2009 [27]	ADI	0–2 μg kg^{-1} bw
Tilmicosin	1998 [28]	ADI	0–40 μg kg^{-1} bw
Triclabendazole	1993 [29]	ADI	0–3 μg kg^{-1} bw
Tylosin	2009 [27]	ADI	0–30 μg kg^{-1} bw
Avilamycin	2009 [27]	ADI	0–2 μg kg^{-1} bw
Endocrine disruptors			
Bisphenol A (BPA)	2015 [30]	TDI	4 μg kg^{-1} bw
E2	2000 [31]	ADI	0–0.05 μg kg^{-1} bw
Testosterone	2000 [31]	ADI	0–2 μg kg^{-1} bw
Progesterone	2000 [31]	ADI	0–30 μg kg^{-1} bw
Melengestrol acetate	2001 [32]	ADI	0–0.03 μg kg^{-1} bw
PFOS	2008 [33]	TDI	150 ng kg^{-1} (bw d^{-1})
PFOA	2008 [33]	TDI	1500 ng kg^{-1} (bw d^{-1})
Polycyclic aromatic hydrocarbons			
Benzo[*a*]pyrene	2006 [34]	BMDL10	0.10–0.23 mg kg^{-1} (bw d^{-1})
	2008 [35]	BMDL10	0.07–0.20 mg kg^{-1} (bw d^{-1})
Chrysene	2008 [35]	BMDL10	0.17–0.45 mg kg^{-1} (bw d^{-1})
PAH[c)]	2008 [35]	BMDL10	0.34–0.93 mg kg^{-1} (bw d^{-1})
PAH[d)]	2008 [35]	BMDL10	0.49–1.35 mg kg^{-1} (bw d^{-1})

Table 1.3 (Continued)

Element/species	Year [Reference]	Type	Value
Brominated flame retardants			
Pentabromodiphenyl ether	2012 [36]	LD_{50}	2640–6200 mg kg^{-1} bw
Polybrominated biphenyls	2010 [37]	LD_{50}	64–150 mg kg^{-1} bw
Hexabromocyclododecane	2011 [38]	NOEL	10 mg kg^{-1} bw
Tetrabromobisphenol A	2011 [39]	BMDL10	16 mg kg^{-1} bw

a) Data taken from Ref. [40].
b) ADI, acceptable daily intake; BMDL, benchmark dose lower limit of the 90% confidence interval; LD, lethal dose; NOEL, no-observed-effect level; PTMI, provisional tolerable monthly intake; PTWI, provisional tolerable weekly intake; TDI, tolerable daily intake; TWI, tolerable weekly intake.
c) Benzo[*a*]anthracene and benzo[*b*]fluoranthene.
d) Benzo[*k*]fluoranthene, benzo[*ghi*]perylene, dibenz[*a*, *h*]anthracene, and indeno[1, 2, 3 − *cd*]pyrene.

The National Secondary Drinking Water Regulations (NSDWRs) comprise guidelines and recommendations for contaminants that are not considered to present a risk to human health. The amount of such substances are quantified as "secondary maximum contaminant levels" (SMCLs) and they represent non-mandatory water quality standards. These contaminants comprise a group of 15 substances that may have an influence on aesthetic considerations, such as taste, color, and fragrances, effects that do not harm the body but are still undesirable such as tooth or skin discoloration or technical effects such as corrosivity and staining related to corrosion, which have remarkable economic implications.

There is a third level that comprises a list of contaminants that are currently not subject to any promulgated regulations, but by virtue of having been detected in public water systems they are listed underthe so-called contaminant candidate list (CCL), following a process that was initiated to develop a regulation (regulatory determination, RD) for a specific contaminant in case it has an adverse effect that would lead it to be included under the SDWAregulations. This institution has developed several lists from 1998, (CCL 1, 2, 4, and 4) (see Figure 1.2).[7]

Table 1.3 shows an example of toxicological guideline values established by European Food Safety Authority (EFSA) and JECFA for some EP classes.

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