



# Introduction

## *A Conceptual and Regulatory Overview, 1800–2000*

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On 20 April 1895, the Frankfurt physician and surgeon Ludwig Rehn (1849–1930) reported at the annual Congress of the German Society of Surgery (Deutsche Gesellschaft für Chirurgie) in Berlin that he had diagnosed three cases of bladder tumors among a group of forty-five workers from the magenta department of one of the largest German aniline dyeworks, at Hoechst on the Main. In the following years, similar cases were found in other German aniline dyeworks, and, as a result, this form of bladder cancer was soon called “aniline cancer.” It was one of the earliest industrial carcinomas diagnosed with certainty. In the century after this discovery, many other industrial chemicals would be shown to be carcinogenic.<sup>1</sup> Magenta had then been produced from aniline on an industrial scale for almost four decades. It was made in dozens of aniline dyeworks all over Europe and the United States. By 1895, some twenty thousand workers were employed in the German dyestuffs industry alone, along with several thousands in other countries.<sup>2</sup>

Why was this particular occupational disease discovered so late? Apart from the obvious possibility that entrepreneurs and physicians connected to these factories might not always have been very keen to publish about the health problems among their workers, there are at least four major reasons. First, we now know cancers such as aniline-induced bladder cancer have a latency period of ten to more than twenty years, so the material properties of substances and organisms matter: the workers diagnosed ill in 1895 had been working with aniline already around 1880. Second, the industry was relatively small in its first ten to fifteen years and only started to employ large numbers of workers after the mid-1870s, so for a long time, the number of affected workers

was simply too small to discover cause-effect relationships. Third, getting occupational cancers is to some degree a matter of chance: some workers are more sensitive to chemicals than others. Finally, only in the course of the twentieth century were statistical-epidemiological data on mortality and morbidity collected systematically on a large scale.<sup>3</sup> Because of these four factors, it would have been difficult to discover aniline cancer before the mid-1890s.

In a nutshell, this example illustrates one of the topics discussed at a workshop that stood at the basis of the present book. Learning processes such as the discovery of new diseases depend not only on the occupational and disciplinary backgrounds of the actors involved but also on processes going on in the material world. In the example given, these material processes include the growing production of aniline dyes and the marked increase in the number of workers involved, but the biomolecular mechanisms that make the metabolites of aniline can also induce cancer in the human bladder.<sup>4</sup> Aniline is just one example among many. Since the Industrial Revolution, numerous new chemicals have been produced industrially in exponentially growing quantities. Today, more than seventy thousand different chemicals are manufactured, thirty to fifty thousand on a significant scale.<sup>5</sup> In most of these cases, the toxic and environmental properties of these substances were unknown when they were introduced to the market and in many cases still are. Often, toxic and other hazardous properties were discovered only after years of production and use. The amount of synthetic chemicals produced today is staggering. Annual production figures in millions of metric tons for some key basic chemicals illustrate this very well: sulfuric acid 230, ammonia 145, ethylene 135, chlorine 65, sodium carbonate 50, and benzene 45, to which almost one hundred million of metric tons of nonferrous metals could be added.<sup>6</sup> All these tons find their way somewhere in society and the environment every year.

For more than two hundred years, industrial societies have struggled to cope with many unknown hazards. In modern knowledge society, there is a permanent tension between innovation and risk. Several chapters of this book illustrate this phenomenon well. Socioeconomic forces and knowledge production give rise to a permanent stream of new products and to growing production units that, in their turn, have unforeseen and initially poorly understood impacts on social life, human health, and the environment. Societies, as well as individuals and groups, have responded to these risks by developing new knowledge on such diverse fields as toxicology, environmental sciences, and

technology assessment; introducing a wide variety of regulatory actions, procedures, and systems; and changing cultural and political attitudes and practices in coping with risk and uncertainty.<sup>7</sup> In recent decades, authors from a broad range of disciplines have written an increasing number of historical studies on toxic and other hazards of industrial societies.<sup>8</sup>

In this volume, we analyze that double-faced interaction between innovation and risk by following a limited number of substances over long periods of time and in different national settings. Over the past twenty years, several such “histories (or biographies) of substances” have been published, thereby illustrating the genre’s epistemological potential.<sup>9</sup> In the following chapters, the historical analysis of several poisonous, or hazardous, chemicals has been combined to provide insights into the interplay between industry, substances, citizens, governments, the environment, and science over the past two centuries. The substances portrayed in depth are the arsenic-containing pigment Schweinfurt green in France and Germany from the late eighteenth century to 1890; lead compounds in France and the United States (1800–1980); aromatic amines in Germany, the United States, and the United Kingdom (1880–1980); dioxins in Germany, the United States, Vietnam, and Italy (1900–1990s); cadmium in Japan (1910–2010); cyclamates in the United States and Germany (1930s–1980s); organophosphates in the United States (1930s–2000); phenoxy herbicides in the United States and Vietnam (1940s–2000); DDT in the United States and the United Kingdom (1945–2000); and MTBE in the United States (1980s–2000s). Although there is a predominance of histories on the health and environmental debates in the United States, interesting comparisons with developments in Germany, France, the United Kingdom, and Japan will help construct the larger picture, which is also the aim of this introduction.<sup>10</sup>

The “biographical approach” of chemical substances looks at the entire “life cycle” of a compound: at its production and uses; at the problems it caused in different realms; at issues of risk assessment, legal control, management strategies, disposal; and, finally, at the development of alternatives. It follows the substance through domains that are usually studied in isolation in the scholarly literature, such as occupational health and safety, food safety, environmental pollution, transport and storage of hazardous substances, agricultural production, and military technologies. This volume aims to shed more light on the interaction between those—legally and institutionally—separated

domains and to trace how borders and interactions between them shifted over time and across national borders. Among those domains, the ones concerned with health issues often figure most prominently in public debates and were among the first to be regulated. We will therefore start with a section on the history of the poison concept. Next, we will discuss how poisons were regulated in the course of history in different social domains. Then, we will address the regulation of hazardous substances and articles in general, excluding the poisons proper, before ending with a brief overview of the book. We will argue that the regulatory fields of both poisonous and nonpoisonous hazardous chemicals had gradually developed by the early twenty-first century toward the regulation of chemicals in general and in Europe especially. On the one hand, this result of a more preventive and precautious philosophy takes serious account of the consequences of uncertainty and risk. On the other hand, it also fits, paradoxically, well into neoliberal policies of deregulation in which economic interests have a greater “say” and are consulted extensively in the implementation of the new legal frameworks. The chemical industry has objected for decades—with a reference to Paracelsus (1493–1541)—to a strict separation between poisonous and nonpoisonous industrial products. That policy seems to have worked out well for the industry.

## Poisons: A Conceptual History

Although poisons and hazards are as old as humanity, “hazardous substances” is relatively new and became popular only after the mid-1970s, when it started to partly replace the older “dangerous substances.”<sup>11</sup> Although some languages translate both concepts as the same term(s) (in German, e.g., *gefährliche Stoffe* or *Gefahrstoffe*), the distinction between the two terms in English is significant. “Hazard” takes into account both danger and risk, thereby including potential dangers of which the actual occurrence is uncertain. The shift from “danger” to “hazard” coincides perfectly with the growing popularity of risk studies and arguments in the 1970s. The category of “dangerous” substances and goods thereafter obtained a narrower meaning in the field of transport.<sup>12</sup> The shift in terminology illustrates a new phase in the conceptual history of chemicals considered dangerous. For many people, the concepts of poison, dangerous substances, and hazardous substances will probably be identical, and, indeed, all the chemicals discussed in

this book were primarily, though not exclusively, a matter of social and political concern because of the suspicion that they were poisonous. However, it is important to realize there is no perfect identity between these concepts. Dangerous and hazardous chemicals are a broad category that, next to poisons, also includes chemicals that are dangerous because they are, for instance, explosive, corrosive, or inflammable. The broader category gradually took shape in the first half of the twentieth century. The concept of poison, by contrast, dates back to antiquity and biblical times, so we will start our overview with a history of the poison concept.

### *Poisons in Antiquity and the Middle Ages*

Most conceptual histories of poison go back to antiquity, where the Greek *pharmakon* (poison) and *toxon* (arrow) and the Latin *venenum*, *virus*, and *potio* are the most relevant terms in this context. *Potio*, for instance, returns in the English and French “poison,” and *venenum* in the French *venin*. Greek and Roman authors mostly classified poisons according to the three realms of nature: animal poisons (from, e.g., vipers and scorpions) received the most attention, followed by plant poisons. Mineral poisons, then, were the least important category.<sup>13</sup> An important dimension of the ancient concept of poison is that it referred both to medicines (“good poisons”) and to magic potions and substances that could kill people or seriously damage someone’s health (“bad poisons”). Some authors relate the difference between the good and bad properties of a substance to differences in quality, whereas others refer to the importance of the quantity involved. Galen and Celsus in some of their writings made a more rigorous distinction between *medicamentum* and *venenum*, the latter being a harmful substance often deliberately applied to murder someone that should be feared. Despite that, the close relation between medicines and poisonous substances was preserved in the Middle Ages, when Arab scholars such as Geber and Avicenna wrote treatises that included both pharmaceuticals and poisons.<sup>14</sup>

### *Poisons, Contagions, and Miasmas*

From the early sixteenth century onward, the concept of poison received a new meaning, mainly because of the impact of the plague and other pestilences on European medicine. Medical authors started

to believe the devastating infectious diseases affecting Europe, such as typhus, syphilis, and the plague, were caused by a poisonous fever, seed, or agent, which the Italian doctor Girolamo Fracastoro (1478–1553) called “contagion.” In the next century, authors such as Guillaume de Baillou (1538–1616) and Thomas Sydenham (1624–1689) reintroduced Hippocrates’s atmospheric miasma theory to account for the occurrence of infectious and other acute diseases, in which noxious vapors emerging from putrescent organic matter, or stagnant water, acted as a kind of atmospheric poison to make people ill. Until far into the nineteenth century, authors of textbooks on poisons and toxicology included contagions and miasmas in their classification of poisons. Alongside the usual categories of animal, plant, and mineral poison, some authors now added aerial poisons, but others preferred to include the miasmas under animal poisons.<sup>15</sup>

In addition, the terms poison (e.g., *venenum* and *virus* in Latin, “poison” in French and English, and *Gift* in German) acquired a stronger negative connotation, which lacked the ambiguity of the Greek *pharmakon*. Although many authors were aware of relations between medicines and poisons, the latter term stood for dangerous substances of death, secrecy, witchcraft, and fear. The often cited, and mostly misunderstood, quote from Paracelsus’s *Sieben Defensiones* (manuscript from 1537/1538, published 1564 as part of the *Drei Bücher*)—“What is there that is not poison, all things are poison and nothing (is) without poison. Solely the dose determines that a thing is not a poison”—seems to have had no impact whatsoever on the medical and pharmaceutical discourses in the early modern period. More importantly, “dose” in Paracelsus’s writings meant something completely different than today. It was a purely qualitative concept, in which terms such as larger or smaller played no role. The “right dose,” for instance, referred to a harmonious equilibrium of forces in nature.<sup>16</sup> The now famous Paracelsus quote was rarely cited before 1900, and it would be another fifty years until it started to be used frequently, by medical men and producers of pesticides or foodstuffs, often for apologetic reasons. The most common idea on the action of poisons in the eighteenth century seems to have been that—similar to the ideas of Cartesians such as Sylvius and Lemery on medicines—the qualities such as shape of the subtle particles of a poison meant that even small quantities could already kill someone via an unknown mechanical force.<sup>17</sup>

### *The Influence of Experimental Physiology and Chemistry*

Around 1800, the concept of poison again changed greatly. The concepts of health and illness in medicine got a new meaning when the dominant humoral pathology gave way to more mechanistic views on the human body. Intertwined with this, developments in physiology and chemistry, as well as the growing importance of toxicological expertise and chemical analysis in forensic medicine, played a role. The use of animal experiments, for instance, by Felice Fontana (1730–1803) and Anton Störck (1731–1803) in the 1760s, followed by the gradual rise of experimental physiology as a branch of medicine after 1800, made it possible to classify poisons not only according to their origin from a realm of nature but also based on a more precise description of their action on organisms, such as corrosive, astringent, paralyzing, or narcotic effects. Also, “dose” had obtained by this time a quantitative meaning. Animal experiments had led to the discovery of a clear relationship between that new concept of the dose of a poison and its physiological effect. By the 1780s, this was only a surmise, but it was for many poisons a widely held scientific view by the 1840s. As a result, the relationship between poisons and medicines became an attractive topic to investigate.

The rise of modern chemical theories in the late eighteenth century, through the influence of Lavoisier and his fellow chemists, did perhaps have an even greater impact on the new way to look at poisons. Instead of being entities of natural history, they were increasingly seen as chemical substances, and the effects of poisons were now understood in chemical, and not mechanical, terms. Part of the new chemistry was the emergence of organic chemistry and the attempts to extract plants’ essential, active, poisonous principles. As a result of experiments by Johann Christian Döhl (1792) and Friedrich Sertürner (1805), poisons were increasingly viewed as physiologically potent chemical substances. All these developments in physiology, animal experiments, chemical theory, and chemical plant analysis found their way in an influential textbook of the young Spanish-French professor of medicine Mateo Orfila (1787–1853), *Traité des poisons tirés des règnes minéral, végétal et animal, ou Toxicologie Générale: Considérée sous les rapports de la Physiologie, de la Pathologie et de la Médecine légale*, published in four parts from 1814 to 1815. This hybrid book marks perfectly the transition from poisons as an object of natural history and forensic medicine to poisons as a chemical and physiological object. Orfila stood, so to speak, with one leg in each approach.<sup>18</sup>

These conceptual changes should therefore not be understood as radical breaks. Knowledge of poisons is not confined to the esoteric circle of one particular scientific discipline, within which paradigm changes can take place, but rather is part of the cultural and social history of humanity, and part of a complex matrix of interacting scientific disciplines. As a result, it is better to visualize these conceptual changes as a kind of sedimentation process in which new layers of meaning are deposited on top of the older ones, whereby the latter are still present. Even after 1800, poisons were still an object of secrecy, danger, fear, and perhaps even mystery for many people. Within the world of eighteenth-century science, poisons and toxicology had primarily been the domain of medical police and forensic medicine, focusing on murder, and that would not really change in the first third of the nineteenth century. So, in disciplinary terms, there was also a strong continuity across the fundamentally new approaches that had been launched around 1800.<sup>19</sup> During the first period discussed in this book, especially in the chapters on Paris green (Mertens) and white lead (Lestel), the concept of poison and the study of toxicology were still very much in flux. It would take the first three-quarters of the nineteenth century before toxicology would change fundamentally into a more experimental and chemical direction, and only by 1900 had the new disciplinary profile of toxicology as an independent scientific field stabilized.<sup>20</sup>

### *Occupational Diseases*

At the end of the eighteenth century, the field of toxicology was the domain of physicians. But when that field moved into a more chemical direction, and especially when new, more complex chemical tests to detect poisons were developed in the mid-nineteenth century, new groups such as pharmacists and the emerging profession of the chemist stepped in. Also, content-wise, the scope of toxicology widened. Traditionally, the study of poisons focused strongly on detection and treatment of criminal acts of poisoning, or accidental acute poisoning. But when the Industrial Revolution gained momentum, increased attention was also given to occupational diseases, often caused by chronic exposure to toxic substances, thereby building on Paracelsus's book *De morbis fessorum metallicorum* about diseases among miners and on Bernardino Ramazzini's (1633–1714) book on occupational diseases among artisans and skilled workers (published in the early eighteenth century and still translated in the mid-nineteenth century). The latter,

with its emphasis on slowly acting chronic poisons, was not part of the traditional literary corpus of toxicology. In the nineteenth century, that separation between occupational medicine and toxicology gradually disappeared, as the role of poisonous workplace substances became a concern. Chronic poisoning, which was hardly an issue for toxicologists in the early decades of the century, now also received attention. Only in the course of the nineteenth century did a clear conceptual distinction between acute and chronic poisoning emerge. John A. Paris and John S. M. Fonblanque (1823) devoted a few pages to “the chronic operation of poisons,” and Robert Christison (1832) mentions chronic poisoning in passing, but only with Alfred S. Taylor (1848) and, especially, Ludwig Hirt (1875) were both forms of poisoning clearly opposed to each other. By 1900, Hirt’s field of industrial toxicology had become a subfield of the study of poisons.<sup>21</sup>

### *Poisonous Gases*

The broadening scope of toxicology, in terms of the different social groups and professions involved, was further widened in the 1850s. The metallurgical and chemical industries had grown to such a scale that the noxious vapors pouring into the atmosphere and the massive pollution of canals and rivers did not escape the population’s attention. The significant, sometimes even massive, public protests in several countries against these evils, and the subsequent advice given by different professional groups in response, offer a unique insight into the views about poisons at the time. The protests were partially directed against the devastating effects of poisonous and noxious industrial waste gases on vegetation. It would be wrong to see this as an early sign of environmental consciousness, although that might have played a role in some cases. Within the legal frameworks of the time, financial interests of farmers and landowners fueled the debates on the impact of the industry on vegetation. Property rights, and loss of property, played a major role. Next to that were serious worries about human health. In 1855, the Belgian pharmacist Léon Peeters published a small brochure entitled *Salubrité publique: Guérison radicale de la maladie des pommes de terre et d’autres végétaux*, in which he argued that the devastating epidemic disease of potato plants that had caused serious famine in Europe in the late 1840s resulted from dangerous vapors of the chemical industry and that small children were suffering from aerial poisons. In the protests and expert testimony that followed these accusations,

an interesting mix can be encountered between purely chemical and toxicological views on gaseous substances such as hydrogen chloride, sulfur dioxide, and nitrogen oxides, and older but still popular views on the roles played by miasmas and contagions in public hygiene. In 1865, the German state physician responsible for the Rhineland, Hermann Eulenberg (1814–1902), summarized these impacts on human health and vegetation in a five-hundred-page textbook on noxious and poisonous gases. Within a mainly physiological structure—in which suffocating gases and three types of toxic gases (narcotic, irritating, biolytic) were distinguished—his approach was primarily chemical, discussing the gases as chemical entities with distinct formulae. Nevertheless, gaseous miasmas and their epidemic consequences were also discussed. The book therefore illustrates quite perfectly the view on (gaseous) poisons during the third quarter of the nineteenth century. At the same time, it also was a milestone at the interface of public health and toxicology, and a specimen of “external” industrial hygiene, which much later would be named environmental toxicology.<sup>22</sup>

Then, as a result of the well-known research from 1870 to 1900 by Louis Pasteur (1822–1895), Robert Koch (1843–1910), and several others including Ferdinand Cohn (1828–1898), John Tyndall (1820–1893), Wilhelm Roux (1850–1924), Martinus Willem Beijerinck (1851–1931), and Dimitri Ivanovski (1864–1920), the ideas on infectious diseases changed completely. Bacteria were discovered, and later viruses. The final publications on miasmas appeared in the 1880s. Toxicology on the one hand, and bacteriology, microbiology, and virology on the other, now followed different paths. The concept of poison changed again. Scientific circles no longer saw it as a cause of infectious diseases, but ideas on miasmas and contagions lingered in other circles. In *Crop Production, Poisoned Food, and Public Health* (1925), the farmer John Hepburn, for instance, argued fertilizer and pesticide use in agriculture was a major cause of cancer, which he considered a contagious disease.<sup>23</sup> By the time Hepburn wrote his book, though, the massive public protests against the chemical industry were something of the past. Why? As we will discuss, most countries introduced some form of factory regulations or made existing regulations more stringent. In most European countries, officers of health and factory inspectors were appointed to control industry; give advice to municipal, provincial, and national authorities; and handle citizens’ complaints. For more than a century, they functioned as a technocratic elite that mediated between government, industry, and the population. Often coming from the same

engineering and scientific schools as the leaders of industry, and from the same social strata, they frequently handled upcoming issues in an industry-friendly manner. Pollution of air, water, and soil continued, although in a somewhat limited way, until the 1960s, when broad public concerns and protests surfaced again.<sup>24</sup>

### *The Threshold Paradigm of Industrial Toxicology*

In the early twentieth century, the study of poisons had, in principle at least, widened itself to the investigation of the toxic properties of almost any chemical substance that was suspected to be dangerous to some degree. In addition to its forensic origins, toxicology had assimilated elements of analytical chemistry (chemical toxicology, toxicological chemistry), pharmacology (animal experiments, the study of drugs' "side effects"), "internal" industrial hygiene (occupational poisoning, industrial toxicology), and "external" industrial hygiene (release of poisonous substances into the atmosphere, surface waters, and the soil). At the same time, it had dissociated itself from the study of infectious diseases.<sup>25</sup> Whereas the development of analytical chemistry and experimental physiology had revolutionized the field of toxicology in the nineteenth century, industry would now take on that role until the 1960s.<sup>26</sup> The number of industry-produced chemicals grew enormously, and their often-unknown toxicological properties posed a risk to workers' health. Industrial toxicology moved center stage, and its paradigm started to dominate the field as whole and how poisons were understood.<sup>27</sup> A key ingredient of that paradigm was the concept of threshold, or limit, value. "Minimal lethal dose" had entered toxicology around 1880 as a quantitative measure to compare the toxicity of different acute poisons. Given the large variation in the response of different test animals of one species, the British pharmacologist John William Trevan (1887–1956), at the Wellcome Physiological Research Laboratories, in 1927 invented the more robust measure LD<sub>50</sub>, the lethal dose at which half the population of test animals in a certain experiment would die. It would play an important role in toxicological research and the regulation of poisonous chemicals until at least the 1980s.<sup>28</sup>

Toxicologists were therefore used to threshold values when industrial toxicologists started to search for the opposite of the minimal lethal dose, namely a maximum allowable concentration. Whereas nineteenth-century labor unions, some medical doctors, and other experts made efforts to ban certain chemicals such as white phosphorus

and white lead from the industry (Lestel; Warren), early twentieth-century industrialists promoted the idea that industrial work would not be dangerous as long as the exposure to chemicals stayed under certain limits. They tried to keep the dangers manageable and avoid a total ban of their products and processes. The idea of safe limits rested on the assumption that organisms, and ecosystems such as rivers, could transform or excrete poisonous substances via their metabolism, as long as the concentration of these substances was not too high. In German debates about river pollution around 1900, Carl Duisberg (1861–1935), a leader of the chemical industry, defended the notion that companies could discharge all their harmful and poisonous wastewaters into rivers, because the rivers’ dilution, as well as their “self-cleaning capacity,” would make the waste harmless. In World War I, two German pharmacologists—Ferdinand Flury (1877–1947) and Wolfgang Heubner (1877–1957)—further developed the key notion of the existence of a safe threshold value working under Fritz Haber (1868–1934) on poison gases, a program in which his “intimate enemy” (*befreundeter Feind*) Duisberg also played a role. Flury and Heubner published their results on hydrocyanic acid in 1919, and other colleagues, including Russian and American industrial toxicologists, took up the notion of threshold values from there. Alice Hamilton (1869–1970), the leading US expert in occupational medicine and industrial toxicology, published *Industrial Poisons in the United States* (1925), the first textbook in the field. After retiring from Harvard Medical School in 1935, she became a medical consultant to the US Division of Labor Standards and as such played a major role in preparing a system of occupational exposure limits, or maximum allowable concentration values, published for the first time in 1947. Animal experiments played a large role in establishing these threshold limit values. Whereas nineteenth-century industrial hygienists had visited the workshops and workers themselves (Mertens), the industrial toxicologists were now largely in the laboratories.<sup>29</sup>

### *Environmental Poisons and Low-Dose Uncertainty*

As is widely known, the 1960s saw an upsurge of environmental concern, the start of a rapidly growing environmental movement throughout the industrialized world, and increased government activity on monitoring and regulating pollution. These concerns did not come out of the blue. In the 1950s, national and international experts had discussed extensively the growing problems of air pollution, the presence of pesticide

residues and toxic dyes in foodstuffs, and worries about pesticides in general (Morris; Stoff and Travis). In the 1960s, all these issues reached the public at large. Rachel Carson's *Silent Spring* (1962) played a major role. A similar spark was ignited by thousands of children born in Germany and elsewhere with severe malformations of their limbs as a result of the pharmaceutical drug thalidomide, which their mothers had taken during pregnancy. Large-scale health disasters in Japan with mercury and cadmium compounds (Kaji), as well as massive air pollution by the then exponentially growing chemical, oil, and steel industries in almost all industrial countries, made the picture complete. Next to Carson's book, Murray Bookchin's *Our Synthetic Environment* (1962), Barry Commoner's *Science and Survival* (1963), and Jerome Rodale's *Our Poisoned Earth and Sky* (1964) reached audiences worldwide. In the same decade, the instrumental revolution in analytical chemistry meant ever smaller amounts of chemical substances could be measured in foodstuffs, human and animal bodies, and the environment. Toxic substances such as PCB, DDT, and dioxins suddenly seemed to be literally everywhere on the globe.<sup>30</sup>

The concerns addressed in the 1960s are still with us. Scanning scientific, activist, and political texts from 1965 to the early 1980s, one can conclude that the concept of poison again changed significantly in at least two ways. "Environmental poison" emerged, with layers of meaning that the older poison concept lacked, and, moreover, growing evidence—though debated—that an exposure to even low doses of certain chemicals could cause serious health problems undermined the dominant threshold paradigm of industrial toxicologists from the 1910s to the 1960s. Terms such as environmental toxicology, ecotoxicology, and environmental poisons, and their equivalents in other languages, entered the literature in the mid-1960s. "Environmental poison" appears to be used with two rather different meanings. On the one hand, the term refers to poisonous substances such as pesticides or other pollutants that are dispersed throughout the environment and pose a danger to human health. To some extent, there is a continuity here with the "external" industrial hygiene of the third quarter of the nineteenth century, although Gerd Spelsberg has argued that smoke and noxious gases were seen in the past mainly as a nuisance that destroyed or devaluated property but in the 1950s were reconceptualized as causing health problems.<sup>31</sup>

On the other hand, "environmental poison" could also refer to substances that poison the (nonhuman) environment. This particular

meaning certainly was a major break with earlier poison concepts that always had been strongly anthropocentric since their ancient origins, even though they had been applied to (other) warm-blooded animals since the eighteenth century. John Prestwich, in *Dissertation on Mineral, Animal and Vegetable Poisons* (1775), defines poisons, for instance, as “those things, which are experienced to be in their whole nature, or in their most remarkable properties, so contrary to the animal life, as in a small quantity to prove destructive to it.” In Johann Friedrich Gmelin’s *Allgemeine Geschichte der Gifte* (1776) and writings of other authors around 1800, we encounter similar definitions. It was Rachel Carson’s concept of the food chain that opened the eyes of the public at large for the poisoning of other forms of life than man and (higher) animals. The German Chemicals Act (*Chemikaliengesetz*) of 1982 aimed to protect both humans and the environment, and required, for instance, toxicological tests on fish, earthworms, water fleas, and algae.<sup>32</sup>

Research in the 1950s and 1960s on the recently discovered mutagenic and teratogenic properties of certain chemicals further widened the concept of poisons, introducing effects not yet discussed in textbooks on forensic and industrial toxicology. New groups of geneticists and toxicologists entered the field, and in the US founded the Environmental Mutagen Society, which successfully acted as an activist pressure group to link mutagens and teratogens to the well-recognized and well-funded problems of cancer research (Schwerin). Mutagens and teratogens also became subject to regulatory measures in the 1970s and 1980s. The Ames test, introduced by the biochemist Bruce Ames (\*1928) in 1973, provided a quick method for testing the carcinogenic and mutagenic properties of chemicals. As a result, research in this area grew exponentially in the following two decades.<sup>33</sup>

This research in genetics also helped undermine the idea defended by chemical companies and industrial toxicologists that toxic chemicals could be handled safely as long as the exposure to humans remained below a threshold limit value. In the 1970s, that idea came under pressure when two research traditions met. On the one hand, as Soraya Boudia has shown, research on the effects of low doses of radiation concluded that the effects were not negligible under any threshold value. Instead, the cumulative effect of low doses of radiation over longer periods could have a serious impact on human health. On the other hand, as argued Alexander von Schwerin, Beat Bächli, and Heiko Stoff and Anthony Travis (this volume), research into the carcinogenic properties of chemicals led to a similar conclusion: in many cases, there was no

minimum safe dose. The defenders of the “old school” heavily contested these results, but when it became clear that they could not be denied, the battle lines shifted to the question of whether the new toxicological insights could be generalized to types of poisons whose mode of action was not based on genetic defects. By 1975, the discussion on poisons was increasingly characterized by terms such as uncertainty and risk.<sup>34</sup>

The broad concept of environmental poisons and the insight that almost all chemicals could have an effect on some organisms, together with the insight that in many cases there might be no safe dose at all, has the potential to completely undermine the traditional notion of a poison. Even though the term poison remained very popular in the press and many public debates,<sup>35</sup> the 1980s can be seen as the end of “era of the poison,” in the sense of the existence of *specific* dangerous substances with unique toxic properties. *Any* chemical substance could form a risk. Because of this blurring of boundaries between chemicals and poisons, we will discuss the regulation in the “risk society” of two more general categories, namely those of hazardous substances and of chemicals in general. However, we will first give a brief historical overview of the regulation of poisonous substances more narrowly conceived, making this broad conceptual overview more concrete by showing in somewhat more detail how poisons were handled in different subsystems of society.<sup>36</sup>

## Regulation of Poisons

Regarding the regulation and governance of risks and dangers, most people will perhaps primarily think of juridical and administrative laws, rules, and regulations. Over the past twenty to thirty years, though, several scholars have argued that a far broader view on issues of regulation is needed to understand how hazards and risks are handled in practice. In the footsteps of Jean-Paul Gaudillière’s studies on the regulation of pharmaceuticals, one can distinguish, for instance, between “industrial,” “professional,” and “public” ways of regulating the uses of poisons, alongside the more well-known “juridical” and “administrative” procedures. Industrial ways of regulating chemicals would include the roles played by business associations on quality control or storage safety, supplying instruction leaflets for (dangerous) products, or surveillance of industrial practices by insurance companies and accountancy firms. Examples of professional regulation are activities of corporations and

scientific associations in collecting and distributing information on health and safety issues, for instance, the making of codices. Public forms of regulation would include activities of consumer groups, the impact of media exposure, or litigation initiated by citizens, to mention a few examples.<sup>37</sup> Given the present state of the historiography of the regulation of poisons, it would be hardly possible to sketch the entire spectrum of regulatory measures over the long period of time discussed in this book. We can only scratch the surface and will mainly focus on regulations of a juridical and administrative nature. But it is good to make the desideratum explicit that further research into other ways of regulating poisons and other hazardous substances should be initiated. On top of that, we will give examples of those other ways of regulation when possible.<sup>38</sup>

### *Pharmaceuticals*

In antiquity (e.g., in Galen's writings), poisons, medicines, and food-stuffs were often mentioned in one breath. They were distinct, but related, because they could all be administered orally. Food could be poisoned, medicines were sometimes too potent and dangerous, and so on. It is therefore perhaps no great surprise that the first explicit regulatory measures on poisons had to do with pharmaceuticals and food-stuffs.<sup>39</sup> The oldest regulations on poisons concerned the apothecary, or pharmacy. This was the place where poisonous chemicals were for sale, and from the fourteenth century onward, many town governments issued prohibitions, sanctions, or ordinances on the selling and storing of poisons. From the eighteenth century onward, common practice ordered poisons be stored in a separate, locked cabinet and all sales of poisons be noted in a special housekeeping book, to be controlled regularly by the town physician.<sup>40</sup> Since the Renaissance, the composition of official drugs made in pharmacies was also regulated by local and, later, national pharmacopoeias. In the mid-nineteenth century, these regulations were amended by acts that tried to prevent the adulteration of drugs, as a result of the advent of industrial medicines and the growing commercialization of the drugs market (e.g., British Pharmacy Act 1868 and the US Pure Food and Drug Act of 1906). Control of narcotic drugs, according to most toxicological handbooks classified as poisons, was stricter and became increasingly regulated internationally from 1906 onward. In that respect, the control for pharmaceuticals and narcotics was a forerunner of the regulation of chemicals in general.<sup>41</sup>

Apart from the standardization of the composition of drugs, many other aspects of pharmaceuticals were not regulated at all for a long time. In the early decades of the twentieth century, there were generally no strict procedures for the admission of drugs, no legal criteria for their efficacy, and no mandatory tests for harmful side effects or for safety. The US Federal Food, Drug, and Cosmetic Act (1938) took a first great step into the opposite direction. The burden of proof for the safety of drugs was put on the shoulders of the manufacturers, and, just as in the case of toxic substances, a precautionary principle (*avant la lettre*) was implemented for pharmaceuticals, although it was abandoned in practice only a few years later.<sup>42</sup> Since the 1930s, the number of new medicines on the market has grown tremendously, leading to an increasing number of cases of poisoning by these new drugs, whose (side) effects were often not well known. Despite these serious signals, the regulation of drugs was not put on a totally new basis until the early 1960s, due to the shock produced by the aforementioned “thalidomide affair.” From 1962, therefore, most countries, with the US Food and Drug Administration in a leading role, considerably tightened up the required testing procedures for drug safety. In the German Federal Republic, the Law on Pharmaceuticals (*Arzneimittelgesetz*) of 1961 was revised again in 1964 as a result of disastrous side effects of thalidomide use. From now on, preclinical and clinical studies became mandatory before new drugs were admitted to the market. In 1976, the West German parliament passed an improved Law on Pharmaceuticals, which came into force on 1 January 1978. Similar laws were established in other countries.<sup>43</sup>

The disastrous effects of thalidomide put, for the first time, the then quite unexpected teratogenic side effects of drugs clearly on the map. After new laws on the admission of novel drugs had been passed in the United States, Germany, and most other developed countries, tests on the teratogenic properties became mandatory, as did tests for the possible toxic, carcinogenic, and (recently discovered) mutagenic effects of drugs. The impact of these ever more stringent regulations on the pharmaceutical industry and on the innovation of new drugs cannot be overestimated. Bringing new drugs to the market became a time-consuming and costly process. Within that force field between risk and innovation, only the largest and most wealthy pharmaceutical companies could keep a stream of innovations flowing, in only by taking over new start-ups.<sup>44</sup>

## *Foodstuffs*

Local regulations on forbidding the use of poisonous substances in foodstuffs also date back to the Middle Ages, but France, as far as we know, was the first country to regulate these issues on the national level. After Louis XIV had issued a general ordinance on the possession of and the trade in poisons in 1682, a 1742 police ordinance on making desserts forbade confectioners from using dangerous colors such as copper and lead compounds in preparing their sweet dishes. Later nineteenth-century regulations on foodstuffs invariably referred back to that eighteenth-century decree on the duties of the police. The law of October 1800 on the police control of the hygiene of cities, including foodstuffs, remained in force during a large part of the nineteenth century, not only in France but also in several countries that had been part of the French empire during the Napoleonic wars.<sup>45</sup> The chapter on Schweinfurt green gives a good insight in the responses of different legal and political regimes on the introduction of that new pigment to the market (Mertens). Within three years after its large-scale introduction in France, the authorities in 1830 issued ordinances that forbade the use of the green coloring matter not only in certain foodstuffs but also in the wrappers around confectionaries. Prussia followed in 1838, but the prevailing statute law afforded less legal possibilities to act in Britain.

For a long time, such legal measures were rather ad hoc, limited to individual products and specific applications. But by the end of the nineteenth century, countries started regulating the quality of foodstuffs more generally on a national basis, not only in view of adulteration practices but also often to protect human health. Whereas the British Sale of Food and Drugs Act 1875 focused mainly on adulteration, the German Food Law (*Nahrungsmittelgesetz*) of 1879 gave more room to health concerns. Apart from foodstuffs, it included other consumer products that could cause dangers, such as toys painted with poisonous pigments. More specific bans of poisonous pigments in foodstuffs and other goods of consumption followed in 1882 and 1887. Similar steps were made in other countries after 1900, for example, the US Pure Food and Drug Act of 1906, which was partly an achievement of the “pure food movement” that had emerged in the United States in the late nineteenth century and later spread to Britain, Germany, and other countries.<sup>46</sup> From the movement’s viewpoint, food additives and pesticide residues in foodstuffs were highly suspicious. When these substances were found, the pure food movement soon labeled these

foodstuffs “poisoned food.” The dangerous aniline dye butter yellow was banned from use in foodstuffs in the United States in 1918.

Stoff and Travis show in their chapter how the debate on “poisoned food,” and butter yellow in particular, evolved in Germany. In 1939, the first German legal measures on food additives were taken. In the 1950s, both in Germany and on the European level, the debate on food additives gained another dimension when it appeared that several of those additives were probably carcinogenic. Butter yellow was forbidden in Germany in 1951. A few years later, the Joint FAO/WHO Expert Committee on Food Additives was created and would play a major role in expert advice on regulations. From 1957 to 1963, “acceptable daily intake” was developed within that body. This concept implied a fundamental break with the earlier practice of using negative and positive lists. It introduced the “threshold paradigm” into the domain of foodstuffs and did not do justice to the suspicion that carcinogenic chemicals could also be dangerous as a result of exposures to low doses. The legal implementation of these ideas differed between countries, though. In 1958, in both Germany and the United States, new food laws, or amendments to existing laws, were enacted that included rules on additives. Because of a specific amendment moved by Senator James Delaney (the “Delaney clause”), “any chemical additive found to induce cancer in man, or, after tests, found to induce cancer in animals” should not be approved for use in food. The clause, therefore, went much further than the JECFA’s proposals, but included an escape for questionable substances that had been used for some time and thus were “generally recognized as safe” (Schwerin). The Delaney clause would be heavily contested for years to come, concerning both the GRAS status of cyclamates and the applicability of the clause to pesticide residues in food (Morris; Schwerin). It played a key role in 1969/1970 in the decision to ban cyclamate use in the United States. In Germany, by contrast, these sweeteners then stayed on the market.<sup>47</sup>

Residues of pesticides in food provoked similar debates. Concern about these residues emerged already well before World War II. However, powerful industrial and agricultural lobbies prevented the creation of strict and binding regulatory measures. In 1963, the Joint FAO/WHO Meeting on Pesticide Residues was established, but regulation continued to diverge greatly between countries. The US Food Quality Protection Act, signed by President Bill Clinton in 1996, finally required a systematic reassessment of all food threshold levels, with respect to residues of organophosphate pesticides in the first place

(Davis).<sup>48</sup> Parallel to these discussions about where to draw the line between “acceptable food” and “poisoned food,” the past few decades have witnessed frequent struggles on the borderline between “health foods” and pharmaceuticals. In Germany, for instance, different rules applied to legal complications of sweeteners used in foodstuffs and in pharmaceuticals (Schwerin). Producers of foodstuffs often advertised products with certain pharmaceutical claims to promote sales and higher margins while simultaneously trying to avoid their products being subject to the strict and extensive procedures of the legislation on pharmaceuticals. Unilever, for instance, first promoted from 1959 to 1961 its cholesterol lowering margarine Becel (Flora in the United Kingdom) only via apothecary shops before launching it as a healthy product in supermarkets. In the past twenty years, the market of “health foods” has grown exponentially, so the EU, followed by other countries, in 2002 tried to draw a clear legal borderline between pharmaceuticals and foodstuffs, thereby solving Galen’s problem in a Solomon-like manner.<sup>49</sup>

### *Transport and Storage*

The trade, transport, and storage of poisonous substances was initially regulated via decrees on the pharmacies and even, in France, via the more general ordinance of 1682. Also, in Germany, proponents of an improved “medical police” such as Johann Peter Frank made a strong case at the end of the eighteenth century for regulating the trade of poisons. Their pleas were successful, because Gustav Kletschke, in 1854, said packing, shipping, and storing of poisonous materials had been sufficiently regulated, at least in the wholesale trade (Mertens).<sup>50</sup> Regulation of issues such as these also extended to the international sphere. At the Congress of Vienna of 1815, the Central Commission for Navigation of the Rhine (CCNR) was created, of which all countries on the then navigable portions of the Rhine became members: Baden, France, Bavaria, Hesse-Darmstadt, Nassau, Prussia, and the Netherlands. After years of rivalry, mainly between Prussia and the Netherlands, an international convention on the navigation on the Rhine was signed in Mainz on 31 March 1831. Under Prussian leadership, in practice at least, the CCNR coordinated and regulated the shipping on the Rhine in the remainder of the nineteenth century. The commission still exists. In July 1838, an agreement was reached on the packing and shipping of arsenic and other inorganic poisons such as quicksilver preparations, sugar of lead,

and Spanish green, and the control thereof. As far as we know, this constitutes the earliest example of an international regulation on poisons, and even on chemicals in general. It stayed in force for many decades.<sup>51</sup>

In the 1870s, tensions between Prussia and the Netherlands grew again. In 1865, the Prussian Minister of Trade had passed an edict that prohibited aniline dye manufacturers from dumping their arsenic waste, resulting from the manufacture of magenta, in rivers. After the opening in 1872 of an improved connection to the sea at Rotterdam, ships with arsenic waste started to sail down the Rhine to dump it into the North Sea. Protests by fishermen led to prolonged negotiations between the Dutch and Prussian governments and finally to the adoption of a Law on the Import, Transit, and Export of Poisonous Substances by the Dutch parliament in June 1876.<sup>52</sup> Concerning storage and transport in non-river environments, for instance, by rail or aircraft, there were many national laws and international conventions, but we will discuss those in the larger framework of the handling of hazardous chemicals in general.

### *Poisons in the Workplace*

Regulations on the dangers and nuisances of industry materials were first mainly limited to the effects they had on factory neighbors, such as stench, smoke, irritation by noxious gases, pollution of wells and rivers, and so on. Although occupational diseases had been known since the times of Paracelsus and Ramazzini, little was done for the workers in terms of legal protection. It was left to the factory owners to decide what measures should be taken to avoid workers becoming ill. There were striking cultural differences between countries regarding labor relations. In the white lead industry, for instance, workers were suffering a great deal from poisonous dust of white lead (Lestel), but while British and later French manufacturers improved the process by breaking the white lead coils under water with special machines, Dutch factory owners only advised workers to protect their noses and mouths with a wet handkerchief and to perform some other tasks every few hours, as a kind of “job rotation.”<sup>53</sup> In the 1860s, the French mining engineer Charles de Freycinet (1818–1923) concluded after a broad survey that the international differences on the regulation of health issues in the workplace were marked. In England, which he visited in early 1863, there was no legal protection worthy of the name. Working conditions differed from factory to factory, depending on the manufacturers’

attitudes. In Belgium and Prussia, state-appointed factory inspectors played an important, positive role, and a lot had still to be done in France, but the manufacturers themselves were improving their processes. The British Alkali Act 1863 was passed to reduce the emission of noxious gases by the heavy chemical industry, and the alkali inspectors appointed as a result changed the situation for the better. The act was modernized several times, and other laws were passed. Nevertheless, as David Walker demonstrated, the situation of workers in dangerous productions was often deplorable until far after World War II.<sup>54</sup>

In their chapters on the Schweinfurt green and white lead industries in France, Joost Mertens and Laurence Lestel both demonstrate how long it took before alarming observations on the health of the workers resulted in legal measures of a binding nature. However, other kinds of regulation played their part, in the form of the distribution of information on dangerous manufactures, technical advice by sanitary committees, procurement policies by the state, and activities by people such as Jean-Pierre Darcet, who tried to reduce workplace dangers by technical means. Due to the prevailing liberal political views, a strong conviction held that manufacturers' self-regulation would be the best way to proceed. Similar regulatory mechanisms were quite successful in the case of producing phosphorous matches. There, the dangerous white phosphorous was replaced gradually from around 1850 onward by the less harmful red phosphorous, on the advice of the Austrian chemist Anton Schrötter (1802–1875). Nevertheless, legal measures to truly prohibit the use of white phosphorous were not taken until the twentieth century. It was banned from the production of matches in the Netherlands in 1901, followed by Germany in 1903. International agreements followed two decades later.<sup>55</sup> Tackling the causes instead of the symptoms often depended on the availability of good and affordable alternatives. After decades of debates in France on the dangers of pigments such as white lead and Schweinfurt green, the use of white lead was finally banned in 1909—though not for self-employed painters—when zinc white and lithopone had become available as alternatives (Lestel).<sup>56</sup> Schweinfurt green, by contrast, despite legal measures taken in 1893 and 1895, remained in use in the shipbuilding industry, where its poisonous properties were in demand for protecting ships' bottoms against algae (Mertens). From 1886 to 1918, measures for the protection of factory workers and painters were also taken in Germany, Britain, Austria, and the Netherlands. In the international arena, the International Labour Organization, established in June 1919, that

actively strove to ban the use of white lead, white phosphorous, and other poisonous substances in industry (Lestel). But ratification of the conventions was often slow. Britain and the United States, for instance, did not sign the White Lead Convention of 1921 to ban the use of white lead from most interiors (Warren).<sup>57</sup>

In 1877 and 1878, Switzerland and Germany were the first countries to pass laws that included provisions for workers' health. Germany was, in 1884, also first to introduce financial compensation for injured workers. Britain followed in 1906. The United States and France introduced similar schemes in the next decade (Lestel; Warren). Initially only intended to compensate income losses as a result of (acute) injuries, it would take many years before chronic occupational diseases were also brought under these laws. That happened in Germany, for instance, in 1925. These laws only applied to workers who became sick from officially recognized occupational diseases. The official listing of an occupational disease could often take several decades after the first alarming symptoms had been discovered (Stoff and Travis). Even then, as Walker shows for Britain, poisoned workers were often just sent home with financial compensation, while the labor conditions were not improved.<sup>58</sup> As discussed earlier as part of the conceptual history of poison, initiatives to ban certain poisonous products were gradually giving way to regulatory policies in terms of threshold values in the interwar years, leading to the MAC values published shortly after World War II. During the same years, an increasing number of workplace chemicals were recognized as causing chronic occupational diseases, such as cancer. All these developments took place mainly within the legal frameworks of factory acts dating from the late nineteenth to early twentieth century. In the 1960s and 1970s, that situation would change, starting with the British Factories Act 1961, the Carcinogenic Substances Regulations 1967, and the Health and Safety at Work Act 1974. The US Occupational Safety and Health Act was passed in 1970, followed in 1976 by the Toxic Substances Control Act (Stoff and Travis). Laws such as these reinforced processes going on within industries to improve working conditions. Nevertheless, the "industrial hazard regimes" differed from country to country and between different industries. Products and processes forbidden in the United States, Europe, or Japan were often still used and practiced elsewhere.<sup>59</sup>

The 1970s were characterized by an increasing turmoil about toxic chemicals, concerning not only the environment and consumers but also the workplace. The number of laws, ordinances, and other

regulations grew steeply. Other regulatory interventions multiplied: increased involvement of labor unions, NGOs, and political parties in health and safety issues; more publicity and public debate; the creation of safety committees inside the factories in which workers now got a voice; and, finally, a growing number of experts from an increasing number of fields who had, or wanted to have, a “say” in issues on toxic chemicals in industry and trade. In clear contrast to the interwar period and the 1950s, experts now often disagreed, for example, on the dangers of prolonged exposures to low doses of carcinogenic chemicals (Schwerin). The robustness of TLVs such as MAC values came into question. In the 1960s, the possible carcinogenic effects of chemicals had already received much attention, but when it became known in January 1974 that vinyl chloride monomer—the starting material for the much-used plastic PVC—had most probably caused liver cancer (angiosarcoma), a “publicity bomb” exploded. After the MAC value of VCM had already been lowered from 500 ppm to 200 ppm around 1970, it now was almost immediately lowered to 50 ppm and, in October 1974 in the United States, even to 1 ppm. Great improvements in the analytical-chemical instrumentation were required to measure levels such as these at all, especially in the less than ideal work atmospheres in the production halls. By 1990, it proved possible to lower VCM concentrations in factories to 0.1 ppm, a fact that puts previous working conditions, when exposures of 3,000 ppm or higher had not been rare, into a poignant perspective. Also, when TLVs in the United States and later Europe had been lowered to 1 ppm, discussions on the dangers of low doses continued, because of not only different theories about the mechanisms of cancer but also different views on precautionary policies in industry (Hay). In the late 1970s and early 1980s, a vast number of books, brochures, and articles on industrial poisons was published, on carcinogenic chemicals in particular.<sup>60</sup> As we will argue, in the 1980s and the decades thereafter, the regulation of toxic workplace chemicals became part of the larger network of legal, political, and public documents and practices on the regulation of chemicals in general.

### *Toxic Pesticides (and Chemical Weapons)*

Many of the substances discussed in this volume are pesticides. As recognized poisons, they were employed *intentionally* because of their deadly effects on organisms regarded as pests in agriculture and for humans. Since the 1870s, pesticides have been released in huge

amounts into the environment. They massively contributed to a growing awareness of hitherto unknown problems connected with the use of poisonous substances.

With few exceptions, the first generations of pesticides used in the nineteenth and the first third of the twentieth century were inorganic compounds, containing heavy metals such as mercury, lead, arsenic, or copper. Their harmfulness to organisms had often been known empirically for centuries; others were byproducts of certain industries such as coal tar dye production. In either case, they were not optimized for application on the farm. Schweinfurt green (Mertens) began to be used as a pesticide as soon as it became clear it was too toxic to be used as pigment. Its first large-scale use was in the United States, where vast monocultures favored the occurrence of pests on mass-produced crops. The regulation of pesticides took the form of advice: users were recommended to apply protective measures known from industrial hygiene—tidiness and cleanliness above all.<sup>61</sup>

Initially, Europe watched these developments in the United States rather skeptically. Germany, however, gave up its reservation against the use of arsenicals as pesticides in World War I due to the lack of other plant protection agents and to the food shortages caused by the war. The fact that the Germans used arsenicals as chemical weapons in the war, as well as the necessity to find new civil utilizations for the production capacities they had built up during the war, played an additional role for the acceptance of arsenicals in agriculture. The history of the first synthetic pesticides is closely connected to the use of poisons for military purposes.<sup>62</sup> The first attempt to regulate the handling of hazardous chemicals on an international level was—significantly enough—directly related to chemical weapons, the use of which had, at least theoretically, already been regulated by the Hague Convention of 1899. After World War I, the international community of states tried to agree on how to handle chemical weapons in the future, leading to the Geneva Protocol of 1925, which did not, however, prevent the development of even more poisonous substances.<sup>63</sup> Furthermore, the history of these new weapons was closely connected to the history of pesticides. A chemist employed by IG Farben, Gerhard Schrader (1903–1990), had been asked to develop new insecticides based on organic fluorine-phosphorous compounds (Davis). By unintentionally poisoning himself in 1937, he became aware of the extreme toxicity of the compound later known as Tabun, produced from 1942 onward. In the meantime, Schrader continued his work on organophosphate insecticides. In 1944,

he finally discovered several substances that could be used as pesticides, among them one that would become known as malathion in the United States.

After World War II, arsenicals were replaced relatively quickly by a second generation of pesticides, the contact insecticides based on organic chlorine compounds. The most prominent example was DDT, the insecticidal properties of which were discovered in 1939. The WHO used DDT as key chemical in its worldwide malaria-eradication programs: it was cheap to manufacture, was easy to use, and had long-lasting effects (Morris).<sup>64</sup> However, already in 1946, it was discovered that mosquitos had become resistant against DDT. Because DDT was highly fat-soluble, it accumulated in organisms, especially those at the end of the “food chain,” a concept that emerged in the DDT discussion. The concerns about the problematic environmental effects of DDT and other chlorinated hydrocarbons found a voice in Carson’s aforementioned *Silent Spring*.<sup>65</sup> The book was a major catalyst for public debates about the dangers of chemicals for people and the environment, as well as for new legislation on the environment in general and pesticides in particular. A few years after the publication of *Silent Spring*, the US government established the National Institute of Environmental Health Sciences (1966) and the Environmental Protection Agency (1970). Other countries founded similar institutions: in West Germany, for instance, the Umweltbundesamt, the equivalent to the EPA, was founded in 1974. Also, legislation on pesticides was adapted to the toxicological and ecological lessons learned in the 1950s and 1960s. In 1962, the Council of Europe created a Working Party on Pesticides, which developed procedures for the registration of these dangerous substances, and since 1963, the FAO and the WHO has held annual joint meetings on pesticide residues. The German *Pflanzenschutzgesetz* of 1968 had similar aims and was followed by ordinances that specified the testing methods and the criteria for accepting new pesticides for entering the market. In 1971, Japan revised its existing Agricultural Chemicals Control Law in the same direction. Four years later, the WHO adopted a classification of pesticides based on their formulation (solids, liquids, aerosols) and their acute and dermal toxicity to rats.<sup>66</sup>

New pesticides were tested not only for their toxic properties but also for their ecotoxicological behavior, which partly depended on their formulation. The new academic discipline of ecotoxicology looked at the mode of action of chemicals and asked about the interaction of pesticides with organisms and ecosystems; the distribution and transport

of these substances over the environmental compartments soil, water, and air; and the impacts on flora and fauna. It was of high symbolic significance that the Nixon administration, when it created EPA in 1970, moved the responsibility for pesticides from the US Department of Agriculture to the new agency. In the same year, Sweden banned DDT use, followed two years later by a ban in the United States (Morris). These bans were partly based on the suspicion that DDT could be carcinogenic. Although that suspicion could not be confirmed (Böschen), governments of many industrialized countries found it necessary to apply what is today known as the precautionary principle, which became an important concept in the legislation on chemicals discussed later.<sup>67</sup> After its ban, DDT was largely replaced by organophosphates, a third generation of pesticides (Davis). Their success was because their properties differed significantly from DDT: they did not accumulate in food chains and were not persistent in the environment. Also, in 1954, a group of carbamate pesticides came on the market. The progression from organochlorine to organophosphate to carbamate pesticides involved an increase in degradability in the environment but at the cost of increased mammalian toxicity. Therefore, scientists concentrated on reducing the mammalian toxicity of the next pesticide generation, which led to the development of neonicotinoids. They came on the market in 1985 but were later discovered to be harmful for bees even at low concentrations.<sup>68</sup>

Closely connected to the history of pesticides and chemical weapons is the history of herbicides (Hay; Böschen). Herbicides based on 2,4-D and 2,4,5-T were developed in the United Kingdom and soon extensively used in US agriculture, but also in the Vietnam War from 1961 to 1970, because of their potential to defoliate trees. They are dangerous, because dioxins are present as contaminants in these products. Agent Orange—a mixture of these two herbicides—contaminated with dioxins was used in Vietnam, leading to severe health effects among Vietnamese and US soldiers. Only after the 1976 dioxin accident in a Seveso chemical plant in Northern Italy did the damage caused by the herbicides to war veterans begin to be discussed in the United States on a larger scale. Because of the Seveso disaster, scientists began investigating the mutagenicity and teratogenicity of dioxins—categories of risks not really regarded as relevant before. In addition, as mentioned earlier, the phenomenon of ecotoxicity was discovered, followed by the discovery of unexpected effects of nonlethal doses on the immune and endocrine systems.<sup>69</sup> Pesticide use played an important role in the

widening of these toxicological debates. Next, we will investigate how the regulation of toxic substances started to be linked to the regulation of hazardous substances more generally and even to the control of chemicals in general.

## Regulating of Hazardous Chemicals

Having analyzed the history of the poison concept, we discussed the regulation of health hazards posed by toxic substances in different domains, such as pharmaceuticals, foodstuffs, transport, workshops, and industries, and, lastly, pesticides. The aim of this section is to place these issues within the larger framework of the regulation of hazardous substances causing non-health hazards—at least, not only health hazards—such as explosions and fires. We will show how, after around 1980, regulations of those types of hazards partly merged in Europe and other developed countries with regulations on poisons, leading to legal frameworks on chemicals in general. “Hazardous substances” or “hazardous chemicals” refer to a broader set of potentially dangerous chemicals than poisons alone. It includes, for instance, flammable materials, corrosive substances, irritating gases, radioactive chemicals, or substances with an unpleasant or disgusting smell. The most influential early law that regulated hazards was the French Empire’s Factory Decree of 15 October 1810 (*Décret impérial relatif aux manufactures et ateliers qui répandent une odeur insalubre ou incommode*) that formed the basis for most nineteenth-century European factory laws. Although smell was the major hazard addressed by the title of the act, a much larger set of potential dangers and nuisances was considered in practice. We will not follow the development of industry legislation in detail here, because we partially addressed it already, but want to highlight the classification of hazards implied by this law that forms an interesting precedent to the classifications we will discuss later.

Napoleon’s Factory Decree was characterized by a combined political-administrative and spatial-geographical type of regulation. Workshops and industry were divided into three categories. The first, most dangerous, class included black powder mills, storage facilities for explosives, gun foundries, ironworks, and, later, town gas factories. As a rule, they had to be situated outside the towns and villages, and only the emperor could give authorization. The second category included most of the chemical industry, and other industries with fire hazards,

such as potteries and distilleries. They were authorized by the prefect of the department or province and could only be situated inside town or villages when the hazards involved were considered small. The factories and workshops in the third, least dangerous, category could be situated anywhere. They had to be authorized by local government. This legal framework dominated the authorization of new factories in Continental Europe for decades. In practice, not only nuisances (smoke, stench, noise) but also health issues (dangerous vapors, effluents, waste) and other dangers (fire, explosions) were taken into account.<sup>70</sup> The regulation of hazardous substances we will discuss can be divided into three categories or legal traditions: regulations on the safety of transport and storage facilities; regulations on the classification and communication of hazardous workplace substances; and regulations on the authorization of hazardous chemicals. Although the first two categories were often related, they had been cast into distinct supranational legal frameworks since the 1950s: the Orange Book on the transport of dangerous goods on the one hand, and the Yellow and Purple Books on the classification, labeling, and packaging of dangerous chemical substances (in the workplace) on the other.

### *Transport and Storage*

The earliest international regulation in this category was the aforementioned agreement on the packing and shipping of arsenic and other inorganic poisons on the Rhine of July 1838. It included not only strict descriptions of how the barrels or boxes with arsenic should be constructed but also rules on labeling. On each barrel or box, “Arsenic (poison)” should be painted with black oil paint. Working with symbols was considered as well. Mertens says in his chapter that Gustav Kletschke proposed in 1854 to paint a black cross on barrels or boxes containing poisons.<sup>71</sup> New laws and regulations were often a response to serious accidents and disasters. In the 1860s, two new substances entered the market that proved to be extremely dangerous: petroleum and nitroglycerine. In view of possible accidents, local authorities acted swiftly under pressure of insurance companies, and a huge petroleum fire in the Port of Antwerp in 1866 stimulated measures on the national and international levels. Within a few years, several local, national, and transnational ordinances and agreements were issued on the handling and storage of these products, for instance, in the Netherlands, as well as within the CCNR. Nitroglycerine, in its turn, was banned from rail

transport, and shipping explosives and inflammable liquids such as petroleum, in the same cargo was prohibited.<sup>72</sup>

Kerosene, then used in lamps, soon became an article of great international trade and commerce, so national and international regulations on safety measures soon came into being. In the 1860s, instruments had already been developed to determine the flash point of petroleum and were soon improved by chemists from France, England, Russia, and the United States. As a result, kerosene and other petroleum fractions became the first products, as far as we know, for which TLVs were defined. When the testing methods prescribed in the British Petroleum Act 1871 were found to be unsound, the chemist Frederick Abel (1827–1902) developed a new instrument to measure the flash point that received mandatory status in the Petroleum Act 1879. For use in lamps, trade/commerce, transport, and storage, the minimum flash point was defined at 23 degrees Celsius, slightly above room temperature. Fractions with a higher flash point were considered safe, and those with a lower flash point hazardous. Other countries adopted similar types of legislation, often with different national instruments and, as a result, different flash points. Also, (inter)nationally operating railway and shipping companies introduced binding rules based on the flash points of the cargo. Later, more refined schemes based on two parameters (the flash point and the boiling point) came into use.<sup>73</sup>

The precautions concerning nitroglycerine were part of more wide-ranging legal frameworks on rail transport. In Britain, for instance, the Railway Clauses Consolidation Act 1845 had removed dangerous goods from the obligation that railway companies should transport all kinds of goods. Due to pressures from the industry, though, railway companies started to transport some dangerous goods from 1855 onward. The issues were finally regulated by the Explosives Act 1875, which adopted a classification of explosives into seven categories and specified the transport regulations of these materials for each class. In 1890, the transport of dangerous goods by rail was for the first time regulated by an international agreement, the Berne Convention. In Britain, from 1892 to 1922, chemists working for the railway companies were heavily involved in developing methods, criteria, and standardized labels for safe transport. One outcome of their work was H. Joshua Phillips's *The Handling of Dangerous Goods: A Handbook for the Use of Government and Railway Officials, Carriers, Shipowners, Insurance Companies, Manufacturers and Users of Such Goods* (1898), showing the entire spec-

trum of actors involved. An updated version of the Berne Convention was issued in 1961, and the US Federal Railroad Safety Act was adopted in 1974. Regulations such as these, however, could not prevent the fact that increased rail transport of chemicals could lead to accidents such as the 1979 Mississauga train derailment, not far from Toronto, from which two hundred thousand people had to be evacuated.<sup>74</sup>

From 1910 onward, the Antwerp branch of the Lloyd's insurance market published guidelines for the maritime shipping of dangerous goods in French, English, and German that went through several editions until the 1960s. On the political level, the first international convention on sea transport—the very general International Convention on the Safety of Life at Sea—was reached in 1929, which included a chapter on all types of cargo (except liquids and gases in bulk) that, “owing to their particular hazards to ships or persons on board, may require special precautions.” Precise agreements on sea transport of hazardous substances, comparable to the agreements for rail transport, were still lacking. There were only many local and national regulations on the loading and shipping of dangerous goods and explosives on ships. On the international level, the Intergovernmental Maritime Consultative Organization and the International Maritime Organization took the lead, developing the International Maritime Dangerous Goods Code (1965) and the Code for the Construction and Equipment of Ships Carrying Dangerous Chemicals in Bulk (1972) that went through many updated editions.<sup>75</sup>

Regarding air transport of dangerous goods, the International Air Transport Association in 1950 took the initiative to issue the first list of recommendations. An improved edition came out in 1956. Around the same time, US and European measures were taken to regulate road transport of dangerous goods, and the handling, transport, and storage of such goods more generally. Various US laws were adopted to regulate such issues, including the Dangerous Cargo Act (1952) and the Hazardous Materials Transportation Control Act (1970). The European Agreement Concerning the International Carriage of Dangerous Goods by Road, the first international agreement that regulated road transport, was adopted in 1957 and regularly upgraded in the next few decades. Moreover, individual European countries also issued national laws and regulations such as the Law on the Transport of Dangerous Goods (*Gesetz über die Beförderung gefährlicher Güter*) of 1975 and the Dangerous Goods Ordinance Road (*Gefahrgutverordnung Strasse*) of 1985 in Germany.<sup>76</sup>

Regulations on the safety of transporting dangerous goods were of course closely linked to issues on the classification and labeling of hazardous cargo. Railway chemists in Britain undertook one of the first attempts to arrive at a more comprehensive classification of dangerous substances in 1892, agreeing on a classification of four types of dangerous goods: explosives, inflammable liquids, dangerous and corrosive chemicals, and miscellaneous. Each category was subdivided according to the magnitude of the hazards involved—the explosives into the seven categories introduced in 1875, and the inflammable liquids, for instance, into categories based on the flash point. On top of that, the committee specified the “conditions of carriage,” forming guidelines on how each material should be stored, packed, and labeled and which precautions should be taken during loading and unloading. By 1914, the British railway companies had adopted a uniform system of labels—consisting of the name of the hazard class and a symbol—that indicated whether a wagon was carrying explosives (circle), inflammable liquids (cross), or dangerous goods (rectangular box).<sup>77</sup>

That British system formed the basis for later international classification and labeling systems intended to improve the safety of transport. An important milestone was reached when the UN published in 1957 the “Orange Book” (*Transport of Dangerous Goods: Recommendations Concerning the Classification, Listing and Labelling of Dangerous Goods and Shipping Papers for Such Goods*), which classified hazardous materials into nine groups: explosives, compressed gases, inflammable liquids, inflammable solids, oxidizing substances, poisonous and infectious substances, radioactive materials, corrosives, and miscellaneous. The Orange Book listed some 2,500 items of commonly carried dangerous goods. This first important international set of recommendations created a framework for more specific regulations for the transport by rail, ship, air, and road and found its way into many countries’ national legislation. In an updated fashion, it remains in force today.<sup>78</sup>

### *Classification and Labeling of Workplace Chemicals*

In the 1950s, attempts were also made to extend these transport rules and regulations to the classification and labeling of hazardous substances in the workplace (factories, laboratories, etc.). The ILO played a crucial role in developing those “communication systems,” especially after World War II. From 1950 onward, the ILO Chemical Industries Committee was busy with classifying and labeling dangerous, obnox-



**Figure 0.1** Illustration of the five symbols for dangerous substances adopted by the Council of Europe in 1962. The symbols for corrosive, explosive, inflammable, oxidizing, and poisonous substances are shown from left to right. The ILO had already proposed four of these symbols in 1952. Source: Rodgers et al., *International Labour Organization*, 123, fig. 3. Published with permission.

ious, and toxic chemicals and, in 1952, proposed five basic symbols for hazardous materials: liquids spilling (corrosion), bomb (explosion), flame (fire), skull and crossbones (poison), and trefoil (radioactivity). However, the UN Economic and Social Council did not adopt this ILO system until 1958. In the following decade, these symbols found their way into the “Yellow Book” for workplace chemicals, which the Council of Europe adopted in 1962. In that document (*Dangerous Chemical Substances and Proposals Concerning Their Labelling*), the symbol for radioactive substances, regulated by a separate convention, was replaced by a symbol for oxidizing agents (see fig. 0.1). It specified the required labeling of five hundred chemical substances frequently used in factories and other workplaces. A few years later, new symbols were added for noxious chemicals and irritating chemicals—for instance, in the EEC Dangerous Substances Directive of 1967. The hazards considered in the Yellow Book and the DSD were related to explosions, fire (oxidizing substances, inflammable substances, highly inflammable substances), health (noxious or unhealthy substances, toxic substances, highly toxic substances), and skin damage (corrosive substances, irritating substances). In the next decade, new pictograms were added for highly inflammable chemicals, highly toxic chemicals, and, finally, environmental hazards. These were incorporated in the recommendations of the International Organization for Standardization.<sup>79</sup>

For the subclassification of certain hazards, TLVs were increasingly used in the twentieth century. The distinction between corrosive and irritating substances in the DSD was still qualitative: corrosive substances destroyed the human tissue, whereas irritating substances “only” caused inflammation. In the case of fire hazards, the flash point criterion had already been used since the late nineteenth century and

divided at first all substances into two classes: flammable and nonflammable. By the 1960s, this had developed into a system with three classes: highly flammable (flash point less than 21 degrees Celsius), flammable (flash point between 21 and 55 degrees Celsius), and nonflammable. In the case of toxic substances such as pesticides, the LD<sub>50</sub> was the usual criterion. In the case of acute oral poisons, the WHO had distinguished four categories since 1975: extremely toxic substances with an LD<sub>50</sub> less than 5 ppm; highly toxic substances with an LD<sub>50</sub> between 5 and 25 ppm; moderately toxic substances with an LD<sub>50</sub> between 25 and 200 ppm; and noxious, or unhealthy, substances with an LD<sub>50</sub> between 200 and 2,000 ppm.<sup>80</sup> In the 1970s, the evaluation, handling, regulation, and management of hazardous materials, substances, and chemicals became a booming field, with its specific conferences, handbooks (e.g., those by James H. Meidl in 1970 and 1972), and scientific journals (e.g., *Journal of Hazardous Materials*, launched in 1975). The paradigm of industrial toxicology—with its rather technical use of exposure models, risk calculations, and TLVs—was the dominant approach, despite growing debates on the effects of low doses and an increased awareness of the role of uncertainties. Regulation of hazardous substances in the last two decades of the twentieth century was characterized by the introduction of an increasing number of hazard categories and of ever more danger classes within each category.<sup>81</sup>

This approach culminated in the Globally Harmonized System of Classification and Labeling of Chemicals developed under the auspices of the UN after the 1992 Rio de Janeiro Earth Summit. The GHS was codified in the “Purple Book” adopted at the 2002 World Summit on Sustainable Development at Johannesburg, together with the Strategic Approach on International Chemicals Management, of which the GHS became a component. The introduction of the GHS did not occur rapidly. Japan and New Zealand adopted the system in 2008, and the EU ratified a new classification, labeling, and packaging legislation based on the GHS in 2009, which replaced the DSD of 1967. The GHS was gradually introduced in practice at the end of 2010 for chemical substances and before June 2015 for mixtures. Instead of five classes for physical hazards, nine for health hazards, and one for environmental hazards, the new UN system distinguished no less than sixteen types of physical hazards, eleven of health hazards, but still only one of environmental hazards. Also, the number of hazard pictograms changed from seven to nine. The six old pictograms stayed more or less the same, but three new symbols were introduced: a gas cylinder, for gases under pressure; an

exclamation mark for harmful substances, dangerous to health, without being a poison; and a torso for health hazards as a result of carcinogenic, mutagenic, or teratogenic chemicals. By putting the last types of hazards in a separate class, apart from the classes of poisons in which they had been included before, the UN finally did some justice to the debates on these types of risks that had taken place since the 1950s.<sup>82</sup> In the past ten to fifteen years, these regulations on the classification and labeling of chemicals have increasingly been related to, and integrated into, the legislation on poisonous substances and to rules on admitting chemicals to the market. We will discuss those recent developments in this volume's conclusion.

## **The Structure and Content of This Book: From Schweinfurt Green to MTBE**

We have divided the chapters of this book into three parts. This division into three clusters is partly chronological and partly thematic. The scientific paradigms and regulatory mechanisms dominant in one period do not suddenly cease to exist during the next one. Hence, the three phases, or parts, are “cumulative.” Issues characteristic for an earlier period still can play a role in the next one, but new insights and procedures begin to be important as well.

### *Part I*

In part I, we have grouped three chapters on pigments and other substances containing lead and arsenic, that were already known to be acute poisons for a long time. There was no doubt those substances were dangerous. So, the toxicological aspects themselves are not the main issue in this cluster, although those aspects certainly played a role in the debates on the hazards of tetraethyl lead in Christian Warren's chapter, in which he extensively discusses Robert Kehoe's theory of “a threshold for lead absorption below which no illness [would] occur.” As a result, the chapters' focus is on the regulation of these poisonous substances in different domains such as food and nutrition, the workplace, homes, and, finally, the environment. Together, these chapters show the importance of the establishment and existence of regulatory and advisory bodies in the nineteenth and early twentieth centuries, with France and Germany being ahead of the United States. These chapters also

demonstrate differences in legal and political cultures, with, according to Joost Mertens, a quite strict separation between French politicians and scientific advisers, as contrasted to a stronger integration of experts within the German state bureaucracies.

Although toxicological issues are generally not prominent on most of pages of part I, and differences between acute and chronic poisoning are not addressed explicitly, they do play a role “between the lines.” Arsenic and lead, and their chemical compounds, were known to be very dangerous acute poisons, but some health effects of a more chronic character were already known by around 1800. But the conceptual distinction between acute and chronic poisoning was only made systematically in the mid-nineteenth century, Alfred S. Taylor’s textbook *On Poisons in Relation to Medical Jurisprudence and Medicine* (1848) being one of the earliest examples. To some degree, the great differences in morbidity between workers in white lead factories and (house)painters, shown in Lestel’s chapter, can also be interpreted as resulting from acute versus chronic poisoning. In the early nineteenth century, white lead workers were sent to hospitals by the dozen each year, and many of them died. By the end of the century, after technological improvements in the factories had reduced the exposure, the public debates shifted to the more gradual and cumulative health problems encountered by painters using white lead. Warren’s chapter mentions other serious consequences of chronic lead poisoning such as illness, or even death, of children under five in the United States, living in houses painted with white lead inside. Since the mid-1960s, the dangers of chronic poisoning by low doses of lead compounds dissipated through the environment—as a result of using TEL in gasoline—were heavily debated again, after Kehoe’s theory had come under attack.

## *Part II*

By contrast to part I, the four chapters of part II address to a much larger degree the discovery of new diseases, health effects, and, as a result, insights in toxicology. Stoff and Travis analyze in their chapter how the carcinogenic properties of chemical substances were discovered and addressed in the first six decades of the twentieth century. Although examples of carcinogenic effects of substances, such as chimney soot,<sup>83</sup> can be identified with hindsight, these effects were absolutely no issue in nineteenth-century toxicology. Only since the late nineteenth century were specific chemicals gradually identified as a possible cause of cancer,

next to radiation and genetic factors. Aromatic amines had the doubtful privilege to be among the earliest suspects, because of bladder cancer found among workers in the synthetic dyestuffs industry, as discussed earlier. It took industrial toxicologists and factory physicians—as early “merchants of doubt”—several decades of debate to agree on which aromatic amines were the most dangerous.<sup>84</sup> As a result, the regulation of these substances mostly occurred after World War II. The related synthetic food colorant “butter yellow” played a key role in that respect. The chapter shows that the substance was important not only in accelerating debates on the regulation of (carcinogenic) food additives but also in the emerging insight that there was probably no threshold level below which carcinogenic chemicals were safe.

In Schwerin’s chapter, food additives also play a central role, now in form of cyclamates sweeteners. The interesting aspect here is that in the 1960s and 1970s, next to carcinogenic effects, mutagenic effects also increasingly received attention, thereby widening the entire spectrum of toxicological effects from acute and chronic effects to totally different types of acute and chronic physiological, histological, cellular, and genetic changes. Schwerin shows the complexity of the issues involved—for instance, of the (assumed) relationships between mutagenic and carcinogenic effects—the role uncertainty played in the debates on these issues, and the influence of the different political cultures in the United States and Germany, leading to contrary outcomes in the regulation of cyclamates. The novelty of the chemical substances involved is not a major issue in part II. Aromatic amines were already produced for decades before the debates of their carcinogenic properties started. Cyclamates, by contrast, were fairly new, but the chapter focuses more on the health effects themselves and regulatory issues.

An even stronger example of an old substance creating new problems is the discovery of the cause of the so-called itai-itai disease in Japan in the early 1960s, as described by Masanori Kaji. The element cadmium had been known for more than 150 years, but by 1960, there were still no systematic insights about its health effects but only scattered reports. The painful itai-itai disease was first described in the 1930s in the basin of the Jinzū River, where a Mitsui Group zinc factory discharged its effluents upstream. But it took another three decades before it could be proved that the cadmium content of the effluents was the major cause of the disease. One of the most fascinating aspects of Kaji’s chapter is how it illustrates the great changes in political culture that took

place in Japan in the 1960s—just as in other highly developed market economies. Although the Mitsui Group experts continued to deny, as they had done in earlier decades, any relation between their effluents and the disease, a special grassroots coalition of victims, lawyers, and physicians, together with some allies belonging to the establishment, won several lawsuits, culminating in 1972 in a total defeat of the Mitsui Group's case. The itai-itai case illustrates well not only the fundamental political changes of the 1960s but also how different professional groups seized the opportunity to team up with the victims and being to act as their spokespersons. Schwerin underlines the same point in the cyclamate debates when he signals the sometimes-opposing views of “agencies, media, politicians, and scientists, all of them claiming to speak for the interests of the consumer.”

Both the role of the 1960s and issues of spokesman ship return in Stefan Bösch's chapter on the changing perceptions of the dangers of dioxins. After decades of obscurity, since around 1900, as an acute and a chronic industrial poison in the electrochemical industry, dioxins in the 1960s and 1970s completely broke out of the confines of industrial toxicology due to their presence as a highly toxic contaminant of phenoxy herbicides (Agent Orange) used in Vietnam, as well as to the Seveso disaster on 10 July 1976. As a result, in the 1980s, dioxins developed into a “total poison,” debated in several arenas, to the degree that only mentioning “dioxins” was enough to end every discussion of the actual risks involved. Bösch also highlights the roles played by uncertainties, analyzed by Schwerin as well, and “non-knowledge,” sometimes used by “merchants of doubt” to avoid regulatory decisions. The extremely high acute toxicity of several dioxins, as well as the great diversity within this family of chemicals, for a long time masked the more complex chronic effects of low doses of these substances, be they carcinogenic, mutagenic, or teratogenic. Because of all these diverse aspects, almost all the issues discussed in part II, and even part I, culminate in Bösch's chapter. Dioxins are the “collective symbols” in which the old and newly discovered health effects come together, because they combine a high acute toxicity with carcinogenicity. Moreover, they shed light on many other hazardous malpractices and “surprises”: think of the role of accidents (Seveso), of side effects of intended uses (Vietnam), and of the global effects of industrial behavior (burning waste, exporting hazards to under-developed countries).<sup>85</sup>

### Part III

Part III focuses on the environmental effects of hazardous chemicals. Although Rachel Carson's iconic *Silent Spring* is also discussed in several of the aforementioned chapters, it plays a key role in this part. Three of the four chapters here specifically discuss the social, political, and natural history of pesticides, which play a great role in Carson's book, and all four are very much focused on the environmental effects of chemicals, a topic put strongly on the map generally in the 1960s, and by *Silent Spring* in particular. Although the environmental and ecotoxicological effects of chemicals to some degree are already foreshadowed in the chapters by Warren, Kaji, and Böschén, they form the overarching topic of part III. The four chapters bring the reader to the start of twenty-first century and all address issues such as environmentalism and political culture that fully unfolded only in the 1960s. In that sense, the long shadow of the 1960s unites them all.

In the first part of Frederick Davis's chapter, the reader is struck by the important role played by sophisticated chemical and toxicological detail and research in the development of the organophosphates. Through taking a step backward, it is important to note this phenomenon unites almost all the chapters of parts II and III. Although scientific expertise played a role in the nineteenth century as well, the huge development in the twentieth century of industrial toxicology, medical science in general, ecology, and, last but not least, chemical analysis with highly sophisticated instruments—as well as the increased specialization and institutionalization of these fields—have fundamentally transformed debates on risk and safety.

The second part of Davis's chapter focuses on organophosphates as problematic successors to DDT, the other "collective symbol" in the domain of hazardous chemicals, next to dioxins (Böschén). DDT, which played a major role in *Silent Spring*, is the subject of a very interesting chapter by Peter Morris in which the "substance histories" of DDT in the United States and the United Kingdom are compared. The differences appear to be huge: in terms of not only the quantities used in agriculture in the first place (the United Kingdom being dwarfed by the United States) but also political culture and regulatory policies. In the United States, the precautionary principle implied by the Delaney clause regarding cancer risks (see Böschén; Morris; Schwerin) played a role, but even more so did the numerous law suits initiated by citizen groups, biologists, environmentalists, and lawyers. In that respect, there

are quite some parallels with the Japanese story told by Kaji, and with Amy Hay's chapter on Agent Orange and other herbicides in which law suits fought by Vietnam veterans are shown to have played an important role. In the United Kingdom by contrast, as Morris argues, backroom negotiations between government officials and various interest groups dominated the scene. Schwerin notes a similar distinction between the United States and, in that case, Germany.

Although the book lacks a specific chapter on the great global atmospheric and stratospheric chemical hazards heavily debated in the past few decades—climate change and the depletion of the ozone layer—the issue lurks around in John Smith's chapter on the fate of MTBE as a gasoline additive in the United States. Introduced in the 1970s as a replacement for TEL as a high-octane component that would not affect the exhaust pipe catalyst, it later grew in importance when the oxygen content of gasoline had to be raised for environmental reasons. In that role, it entered into competition with bioethanol, which finally won the battle for political reasons, Smith argues, because assumptions about the greenhouse effect sparked the desire for an allegedly renewable fuel. Smith also nicely shows how the economic interests of corn and sugar producers played a role in the MTBE debates, a topic foreshadowed in Schwerin's chapter when he addresses the role of sugar producers in discussing cyclamate sweeteners in the United States. That does not mean, of course, the importance of industrial lobbies is limited to the United States. One could argue the role of litigation in the US system, as well as the local interests defended by senators and other politicians, make that role in the United States just more visible. For a long time in Europe, these influences were more hidden because of informal, confidential consultation and backroom negotiations. As the example of the REACH legislation shows, discussed in our conclusion, industrial interests and lobbies are now very present in Europe.

This brief discussion of some important aspects of the chapters of this book, without discussing all their rich details, suffices to demonstrate that the book as a whole gives a broad and interesting picture of the changing ways in which societies coped with chemical hazards. In our conclusion, we will return to some of these issues and analyze the outcomes of the chapters chronologically in relation to important recent studies. We will then also discuss more explicitly the differences and similarities between the three parts.

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## Notes

1. Rehn, “Blasengeschwülste”; Berenblum, “Aniline Cancer”; Schmähl, “Krebserzeugende Stoffe”; Blackadar, “Historical Review.” See also Stoff and Travis, this volume.
2. Haber, *Chemical Industry*.
3. Struyker Boudier et al., *Risiko’s meten*, 37–55.
4. For a theoretical reflection on, as well as the empirical study of, relations between material processes and knowledge production, see Latour, *Pasteurization*; Vries, *Bruno Latour*, 53–81.

5. Gelbke and Fleig, "Entwicklung," 303–4; Lönngren, *International Approaches*, 19–20; Führ, "REACH," 110; Langston, "New Chemical Bodies," 260; Golding, *History*, 96.
6. See the page "Basic Chemicals" of "The Essential Chemical Industry—Online", last consulted 31 March 2019, which lists the most important chemicals and their production figures. <http://www.essentialchemicalindustry.org/chemicals.html>. For historical figures, see Goertz, *World Chemical Industry*; Reuben and Burstall, *Chemical Economy*.
7. Bora, Henkel, and Reinhardt, "Einleitung"; Versluis et al., "EU Seveso"; Böschen, "Risikogenese"; Scheringer et al., "Will We Know," 700.
8. For references to literature from the 1970s to the 1990s, see Homburg, "Industrie"; Homburg, "Schrikbeelden"; Homburg, "Pollution." For reviews of recent literature on toxicants and regulation, see Jas, "Chemicals"; Guillem-Llobat, "Science"; Bertomeu-Sánchez and Guillem-Llobat, "Following Poisons"; Demortain, "Expertise"; Kirchhelle, "Toxic Tales."
9. Simon, *DDT*; Ball, *H<sub>2</sub>O*; Whorton, *Arsenic Century*; Böschen et al., "Stoffgeschichten"; Chang and Jackson, *Element*; Hahn and Soentgen, "Acknowledging Substances," 19–33.
10. An even broader view can be obtained by considering the "substances histories" that were presented at the same conference on which this book is based but have been published elsewhere. Erker, "Hazardous Substances" (on quicksilver, benzene, asbestos, organobromine compounds, carbon dioxide, picloram, and Agent Orange); Tyabji, "Hazard Concerns." For a recent history of toxic substances and pollution in a non-Western country (India), see Arnold, *Toxic Histories*.
11. Based on searches in large (national) library catalogs on these terms.
12. Boudia, "Managing Scientific." Today, "dangerous goods" is limited to transport regulations, although "hazardous materials" is more common in that field in the United States. "Dangerous goods" is in some respects narrower than "hazardous chemicals" (namely, now, only relating to transport and, mainly, acute dangers), and in other respects broader (namely, articles such as air bags and lithium batteries, as well as radioactive substances, that are mostly regulated separately). See CSP, "Differences."
13. Stevenson, *Meaning*, 1–22; Wahrig, "Gift," in *Literatur*; Dilg, "Griechischen."
14. Mead, *Mechanical Account*, 131–32; Steinschneider, *Toxikologischen Schriften*; Kuhlen, "Gift"; Kreek, "Alexander Willem Michiel," 6.
15. Kessler, *Nützlich und tröstlich*; Wood, *From Miasmas*, 1–23; Bynum et al., *Dictionary*, 75–76, 409, 428; Fischer-Homberger, *Medizin*, 361–64; Montfort, "Venenum," 309–23; Wahrig, "Organisms"; Crowther, "Toxicology"; Mead, *Mechanical Account*, 149–83; Hunter, "Of Poisons."
16. Montfort, "Venenum"; Gmelin, *Allgemeine Geschichte*, 18–21; Deichmann et al., "What Is There"; Ickert, "Von der rechten Dosis"; Papadopoulos, "Gift."
17. Mead, *Mechanical Account*; Halle, *Gifthistorie*, 2; Wahrig, "Gift," in *Enzyklopädie*; Sudhoff, *Versuch*, 100–101; Paracelsus, *Sieben Defensiones*, 8, 25;

- Stadlinger, “Paracelsus,” 349; McLean, “Pesticides,” 614. The only historian, as far as we know, who related late eighteenth-century discourses on doses directly to the ideas of Paracelsus is Esther Fischer-Homberger, but she does not give any direct evidence for that link or seem to have realized that Paracelsus’s concept of dose was totally different from the eighteenth-century notions. See Fischer-Homberger, *Medizin*, 377–78, 393–95, 401, 406.
18. Plenk, *Toxikologie*, 11; Paris and Fonblanque, *Medical Jurisprudence*, 131; Fischer-Homberger, *Medizin*, 395–99, 402–6; Earles, “Experiments”; Kreek, “Alexander Willem Michiel,” 7–13; Wahrig, “Zeit”; Wahrig, “Organisms”; Crowther, “Toxicology”; Wahrig, “Geheimnis”; Bertomeu-Sánchez et al., *Chemistry*. See also Watson, *Forensic Medicine*.
  19. Schneider, *Ueber die Gifte*; Marx, *Lehre*; Christison, *Treatise*; Wahrig, “Erzählte Vergiftungen”; Wahrig, “Geheimnis.”
  20. We refer to this book’s chapters by mentioning the name(s) of the author(s) in in-text parentheticals.
  21. Ramazzini, *Abhandlung*; Paris and Fonblanque, *Medical Jurisprudence*, 143–49; Christison, *Treatise*, 162, 207, 364–65; Taylor, *On Poisons*, 98–99; Hasselt, *Handbuch*; Hirt, *Gewerblichen Vergiftungen*, esp. 3–4, on the distinction between acute and chronic poisoning; Weichardt, “Gewerbetoikologie,” 198–206; Wahrig, “Organisms”; Crowther, “Toxicology”; Wahrig, “Geheimnis”; Reinhardt, “Expertise”; Friedrich, “Apotheker”; Whorton, *Arsenic Century*, 174, 188–92. Joseph Adams (*Observations*), building on earlier ideas by Thomas Sydenham and John Hunt, distinguishes between chronic and acute but refers to diseases, not to the contagious poisons themselves.
  22. Boens, *Étude hygiénique*; Eulenberg, *Lehre*; Spelsberg, *Rauchplage*; Homburg, “Schrikbeelden”; Wilmot, “Pollution,” 121–47. Although the mid-nineteenth century views were ambiguous, some actors, such as Eulenberg, also saw the nuisances and toxic effects caused by some gases as a chemical affair. We therefore disagree with Rachel Rothschild (“Turn towards Toxins”), who argues the “toxic fog” of December 1930 in the Meuse Valley was the historical turning point for understanding chemicals as toxic.
  23. Hepburn, *Crop Production*; Wood, *From Miasmas*, 29–32, 37–40, 95; Bynum et al., *Dictionary*, 22–23, 39, 75–77, 200; Fischer-Homberger, *Medizin*, 378; Langston, “New Chemical Bodies,” 261.
  24. Spelsberg, *Rauchplage*, 205–14; Homburg, “Schrikbeelden”; Homburg, “Pollution”; Walker, “Occupational Health,” 33–36, 155–56, 238–40, 265–66; Zimmer, “Brouillard”; Zimmer, “Dodelijke nevels”; Rothschild, “Turn towards Toxins,” 128; Newman, *Love Canal*.
  25. Lewin, *Lehrbuch*, iii–v; Mohr, *Chemische Toxicologie*; Kobert, *Lehrbuch*; Baumert, *Lehrbuch*; Lewin, *Gifte*; Kreek, “Alexander Willem Michiel,” 14; Wahrig and Neubaur-Stolte, “1929”; Bertomeu-Sánchez, “From Forensic,” 92.
  26. Mohr, *Chemische Toxicologie*; Bertomeu-Sánchez et al., *Chemistry*; Reinhardt, “Expertise.”

27. Moeschlin, *Klinik*, preface; Walker, "Occupational Health," 152, 155; Wahrig and Neubaur-Stolte, "1929," 83; Scheringer et al., "Will We Know," 700; Boudia, "From Threshold." See also Langston, "New Chemical Bodies," 260.
28. The date 1880 is based on a search for "minimal lethal dose" in Google Books. See Trevan and Dale, "Error"; Gaddum, "John William Trevan"; Leake, "Scientific Status," 2073.
29. Hamilton, *Industrial Poisons*; Hamilton and Johnstone, *Industrial Toxicology*; Cage, "Development," 227; Moeschlin, *Klinik*, 37–45; Lönnngren, *International Approaches*, 23, 43; Weichardt, "Gewerbetoxikologie," 206–8, 217–18; Gelbke and Fleig, "Entwicklung," 327–28; Andersen, "Pollution"; Reinhardt, "Limit Values"; Sellers, "Cold War," 25–45; Langston, "New Chemical Bodies," 260–61; Plumpe, *Carl Duisberg*, 466–80, 661–70. See also "Haber's Rule," Wikipedia, last edited 4 October 2018, 16:51, [https://en.wikipedia.org/wiki/Haber%27s\\_rule](https://en.wikipedia.org/wiki/Haber%27s_rule).
30. Carson, *Silent Spring*; Briejèr, *Zilveren sluiers*; Spelsberg, *Rauchplage*, 205–14; Lönnngren, *International Approaches*, 28, 45–48, 60–62, 66–67; Tesh, *Uncertain Hazards*, 43–49; DeSombre, *Domestic Sources*, 81–88; Böschén, *Risikogenese*, 266–76; Morris, "Parts per Trillion"; Forths et al., "Arzneimittel," 65–68; Kirk, *Contergan-Fall*; Botting, "History"; Jas, "Adapting." See also Stoff and Travis, Schwerin, Morris, Kaji, and several other authors, this volume.
31. An illuminating study of the rise of ecotoxicology that addresses the change in focus from humans to nonhuman biota, is Halfman, *Boundaries*, esp. 116–17, 157–58, 167, 322–23, 413–18. See also JMPR, *Evaluation*; Spelsberg, *Rauchplage*, 209–10; DeSombre, *Domestic Sources*, 81–88; Langston, "New Chemical Bodies," 262–63.
32. Prestwich, *On Mineral*, 1; Gmelin, *Allgemeine Geschichte*, 22; Schlemper, *Over den invloed*; Matsumura et al., *Environmental Toxicology*; Engelhardt and Lange, *Chemikaliengesetz*, 22–24; Andersen, "Pollution," 196–97; Böschén, *Risikogenese*, 276–301; Wahrig, "Organisms," 162–63, 179.
33. Creager, "Political Life," 46–64.
34. "ACS Updates Environmental Report," *Chemical & Engineering News*, 56, no. 49 (1978): 34–36; Reinders, *Risico's*; Tesh, *Uncertain Hazards*; Schwerin, "Low Dose Intoxication," 401–18; Bächli, "Zur Krise"; Reinhardt, "Limit Values," 596; Scheringer et al., "Will We Know," 700; Jas, "Adapting," 64–65; Boudia, "From Threshold"; Boudia, "Managing Scientific." An early example of risk concept is Weisburger and Weisburger, "Chemicals," 124–42.
35. Cf. Margerison et al., *Superpoison*; Hemminger, *Vorsicht Gift*; Henseling, *Planet*.
36. Beck, *Risk Society*; Lönnngren, *International Approaches*, 21; Bora, Henkel, and Reinhardt, "Einleitung."
37. Schot, *Geven*; Gaudillière and Hess, *Ways of Regulating*; Gaudillière, "DES," 91; Bora, Henkel, and Reinhardt, "Einleitung"; Demortain, "Expertise."
38. For an overview, see Boudia and Jas, "Introduction," 3–14; Boudia and Jas, "Gouverner."

39. Kuhlen, "Gift," 1446; Steinschneider, *Toxikologischen Schriften*, 16–18.
40. Lenihan and Fletcher, *Chemical Environment*, 99; Wahrig, "Stoff der Macht," 311–12; Wahrig, "Erzählte Vergiftungen," 100–101; Fischer-Homberger, *Medizin*, 79, 96, 98; Gelbke and Fleig, "Entwicklung," 341–42.
41. Rücker, "Langer Weg"; French and Phillips, *Cheated*, 34; Weber, *Food*; Lönngren, *International Approaches*, 22–23, 30, 47–49.
42. Gelbke and Fleig, "Entwicklung," 297–98; Brosnan, "Law," 538; Langston, "Precaution," 30–31; Gaudillière, "DES," 68.
43. Moeschlin, *Klinik*, preface; Homburg, "Era," 437; Le Fanu, *Rise and Fall*, 211–20; Forth et al., "Arzneimittel"; Gelbke and Fleig, "Entwicklung," 341–44; Rücker, "Langer Weg"; Kirk, *Contergan-Fall*; Jungmayr, "Contergan-Tragödie"; Blasius, "25 Jahre"; Schmidt, "50 Jahre"; Johnson et al., *Thalidomide Catastrophe*.
44. Chandler, *Shaping*, 239–56; Homburg, "Era," 544–51. On the actual European practice of regulation, see Hauray, "From Regulatory Knowledge."
45. Gelbke and Fleig, "Entwicklung," 313–14; Fischer-Homberger, *Medizin*, 96; Hartman, *Bestuur*, 299–302.
46. French and Phillips, *Cheated*, 1, 5, 34–37, 112; Baumert, *Lehrbuch*, 27, 30; Dennstedt, *Chemie*, 400–403; Hahn and Winters, "Neuordnung," 399; Vaupel, "Arsenhaltige Verbindungen," 40; Weber, *Food*, 1, 14; Gelbke and Fleig, "Entwicklung," 314, 341–43.
47. Hepburn, *Crop Production*; Bogaers, *Blaastumoren*, 60; French and Phillips, *Cheated*; Gelbke and Fleig, "Entwicklung," 314–15, 327; Lönngren, *International Approaches*, 68–70; Jas, "Adapting," 49–65.
48. Langston, "New Chemical Bodies," 262–71; Jas, "Adapting," 49.
49. Helvoort et al., *Gesmeerde kennis*, 39–42; Hahn and Winters, "Neuordnung," 398–99.
50. Fischer-Homberger, *Medizin*, 96, 98.
51. Klemann, "Central Commission," 35, 37, 39, 46–47; "Reglement betrekkelijk den vervoer van Arsenicum en andere metaal-vergiften: Aanhangsel van het protocol no. XVII van 24 julij 1838," *Staatsblad van het Koninkrijk der Nederlanden* 1 (1844): 16–18; Hartman, *Bestuur*, 53.
52. Andersen, "Pollution," 186–89; Graaff, "Milieuvervuiling."
53. Müller, *Paracelsus*; Homburg and Vlieger, "Victory," 38; Weichardt, "Gewerbetoxikologie," 220–24.
54. Freychinet's reports were published in several issues of the *Annales des Mines* vols. 5–10 (1864–1866). For the final report, see Freychinet, *Traité*. Walker, "Occupational Health."
55. Graham, "Class II," 92; De La Rue and Hofmann, "Class XXIX," 1410–12; Schrötter and Anthon, "Classe II," 84–89; Hahn and Winters, "Neuordnung," 399; Lönngren, *International Approaches*, 23, 43. For conflicting views on the role of Darcet, see Le Roux (*Laboratoire*, 305–448; "Governing," 76–78), who points to Darcet as a key chemist and industrialist who "liberalized" (i.e., weakened) the traditional industrial regulations in the interests of industry,

- and Jorland (“Review”), who emphasizes his role as technical innovator, also with positive effects for workers and neighbors.
56. See also Rainhorn, “Santé.”
  57. Fuchsloch, “Blau—Weiss,” 213–14; Lenihan and Fletcher, *Chemical Environment*, 68–70, 76–77; Walker, “Occupational Health,” 33; Lönngren, *International Approaches*, 23, 38, 41–43; Golding, *History*, 145–46.
  58. *Cinquième congrès international d’hygiène et de démographie à La Haye (du 21 au 27 août 1884): Comptes rendus et mémoires, publiés par le secrétaire général avec le concours de MM. les Secrétaires de Séances et MM. les Secrétaires des Sections*, vol. 2 (The Hague, 1884–1885), 209–14; Weber, *Arbeitsicherheit*, 17, 19, 103–4; Walker, “Occupational Health”; “Bekanntmachung über die Gewährung von Sterbegeld und Hinterbliebenenrenten bei Gesundheitsschädigung durch aromatische Nitroverbindungen,” *Reichsgesetzblatt*, 12 October 1917, 900; Weichardt, “Gewerbetoxikologie,” 208–14; Gelbke and Fleig, “Entwicklung,” 341–43; Bächli, “Zur Krise,” 419.
  59. Lenihan and Fletcher, *Chemical Environment*, 58; Walker, “Occupational Health,” 34, 117–18, 121, 150, 155–57, 241–42; Bogaers, *Blaastumoren*, 45–46, 79–80; Weichardt, “Gewerbetoxikologie,” 212–17; Sellers and Melling, *Dangerous Trade*.
  60. Gelbke and Fleig, “Entwicklung,” 300, 341–44; Walker, “Occupational Health,” 157; Levinson, *PVC*; Homburg, “Era,” 369–73; Markowitz and Rosner, *Deceit and Denial*, 178–233; Krinsky, “Low-Dose Toxicology”; Golding, *History*, 152–59.
  61. Vaupel, “Arsenhaltige Verbindungen,” 44–58; Weber, *Food*, 32; Gelbke and Fleig, “Entwicklung,” 342.
  62. See Russell, *War and Nature*.
  63. Lowe, *International Protection*; Rodgers et al., *International Labour Organization*.
  64. Lönngren, *International Approaches*, 27, 47–48, 55–57; Kinkela, *DDT*, 7, 15–21, 28–29; Vaupel, “Arsenhaltige Verbindungen,” 60.
  65. Lear, *Rachel Carson*.
  66. Lönngren, *International Approaches*, 28, 48, 51, 55–66, 72–74; Vaupel, “Arsenhaltige Verbindungen,” 44, 50, 52, 57, 62; Gelbke and Fleig, “Entwicklung,” 312–13, 341, 343; Weber, *Food*, 1.
  67. Roberts, “Unruly Technologies,” 256–57; Rosner and Markowitz, “Industry Challenges.” For a history of ecotoxicology, see Halfman, *Boundaries*.
  68. Goulson, “Review.”
  69. Schug, “Minireview.”
  70. Koelma, *Handboek*, 4–6; Hartman, *Bestuur*, 179–81; Coronel, *Gezondheidsleer*, 16–20; Homburg, “Schrikbeelden,” 440–51; Le Roux, *Laboratoire*; Klein, “Risques industriels,” 260–65; Jarrige and Le Roux, *Contamination*, 92–102.
  71. “Reglement betreffende den vervoer van Arsenicum.”
  72. Koelmans, “Van pomp,” 10–21, 24–26, 50; Hartman, *Bestuur*, 62, 128–29, 182, 223.

73. Forbes and O'Beirne, *Technical Development*, 57; Peckham, *Report*, 220, 223–37; Wischin, *Vademecum*, 88–95; RDSG, *Petroleum Handbook*, 176–77; Koelmans, “Van pomp,” 50.
74. Lönnngren, *International Approaches*, 78–80, 85; Russell and Hudson, *Early Railway Chemistry*, 151–63; Gelbke and Fleig, “Entwicklung,” 343; “1979 Mississauga Train Derailment,” Wikipedia, last edited 17 January 2019, 17:24, [https://en.wikipedia.org/wiki/1979\\_Mississauga\\_train\\_derailment](https://en.wikipedia.org/wiki/1979_Mississauga_train_derailment).
75. Aeby, *Dangerous Goods*; Lönnngren, *International Approaches*, 40, 80–81, 86.
76. Lönnngren, *International Approaches*, 78, 80; Gelbke and Fleig, “Entwicklung,” 342–43.
77. Russell and Hudson, *Early Railway Chemistry*, 152–61.
78. EC, *Chemicals*, 7–8.
79. Lönnngren, *International Approaches*, 27, 78–86; Rodgers et al., *International Labour Organization*, 122–23; “Richtlinie des Rates vom 27. Juni 1967 zur Angleichung der Rechts- und Verwaltungsvorschriften für die Einstufung, Verpackung und Kennzeichnung gefährlicher Stoffe,” *Amtsblatt der Europäischen Gemeinschaften* 10, no. 196 (1967): 1–98; Seidl, “GHS.”
80. Lönnngren, *International Approaches*, 63–64, 78–79; Seidl, “GHS.”
81. Reinhardt, “Regulierungswissen,” 351.
82. Fischer, “International einheitlich”; Darschnik, “Stolperstellen”; Jeschke, “Sicherheit koordinieren”; Karavezyris and Koch-Jugl, “Globale Chemikalien-sicherheit”; EC, *Chemicals*; Seidl, “GHS.”
83. Brown and Thornton, “Percivall Pott.”
84. Oreskes and Conway, *Merchants of Doubt*.
85. Cf. Sellers and Melling, *Dangerous Trade*, 202–5; Kirchhelle, “Toxic Tales,” 219–20; Jas, “Chemicals,” 195–96; Jas, “Gouverner,” 53–60.

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