Since World War II, synthetic chemical pollutants have accumulated in the environment and food webs on a global basis, have damaged wildlife populations, and may pose large-scale hazards to human health. Despite the global nature of this problem, the vast majority of environmental regulations focus on preventing local risks using risk assessment of individual compounds, discharge permits, and control and disposal technologies. The current approach has failed to prevent global contamination and environmental damage because it underestimates the scale, complexity, and diversity of the hazards of chemical pollution. Fundamental shifts in the mode of chemical assessment and policy are required; a new framework should focus on chemical classes rather than individual substances, convert industrial processes to prevent the production and use of persistent and/or bioaccumulative substances, and shift the default state of pollution policy in the face of uncertainty from permission to restriction.*

Key words: chemical pollutants; global pollution; regulations; risk assessment; public policy; persistent organic pollutants.

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At the time of this writing, the nations of the world are negotiating the first legally binding instrument to address global contamination by persistent organic pollutants (POPs). Motivated by growing evidence that diverse mixtures of synthetic chemical pollutants are now globally distributed in the environment and food web, have damaged wildlife populations, and have the potential to cause large-scale human health damage,1,2 the POPs agreement has the potential to establish a framework for effective action on an environmental issue of profound consequence.

The draft agreement,3 however, manifests a deep tension between the established—and largely ineffective—risk paradigm for addressing global contamination by persistent organic pollutants (POPs). Motivated by growing evidence that diverse mixtures of synthetic chemical pollutants are now globally distributed in the environment and food web, have damaged wildlife populations, and have the potential to cause large-scale human health damage,1,2 the POPs agreement has the potential to establish a framework for effective action on an environmental issue of profound consequence.

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The modus operandi of the risk paradigm is to manage pollution by permitting chemical production, use, and release, as long as discharges of certain individual substances do not exceed some quantitative standard of acceptable contamination. The belief that health and ecosystems can be protected in this way is founded on two central assumptions: that ecosystems have an “assimilative capacity” to absorb and degrade pollutants after they have been created, on a local scale. On the other, it would initially address just 12 pollutants, most of which have already been restricted by many of the world’s nations, ignoring thousands more POPs in commerce or produced accidentally. And for several of the 12 chemicals, whether the treaty will require their generation to be eliminated or merely reduced by improving control and disposal technology remains unresolved and a matter of controversy.

The purpose of this paper is to show that the agreement will adequately address the global POPs problem only if it moves decisively away from the dominant regulatory approach. The goal of the POPs negotiation process should be to establish a framework for a precautionary mode of environmental management focused not on controlling a list of individual substances but on eliminating broad classes of hazardous chemicals and the technologies that produce them.

THE RISK PARADIGM

In the 1970s, industrialized countries adopted a framework for assessing and regulating toxic chemicals that remains largely in force today. I call this approach the risk paradigm, because it views environmental hazards as “risks”—locally bounded, short-term, probabilistic events—and it uses risk assessment as its primary scientific and policymaking tool. It is a paradigm, in the sense of Kuhn,4 because the scientific and political assumptions, concepts, and tools that make up the risk paradigm determine how data on the sources and impacts of toxic chemicals are collected and interpreted, how conclusions are drawn from them, and what kinds of action will be taken in response.

The modus operandi of the risk paradigm is to manage pollution by permitting chemical production, use, and release, as long as discharges of certain individual substances do not exceed some quantitative standard of acceptable contamination. The belief that health and ecosystems can be protected in this way is founded on two central assumptions: that ecosystems have an “assimilative capacity” to absorb and degrade pollutants with-
out harm, and that organisms can accommodate some
degree of exposure with no or negligible adverse effects,
so long as the exposure is below a “threshold” of toxicity.

As implemented, the central artifact of the risk para-
digm is the pollution permit—a license that sets maxi-
mum legal release rates of individual toxic chemicals
from individual facilities. (The same approach is manifest
in acceptable pesticide residues in food and legal limits
for workplace exposures to individual toxic substances.)
These limits are calculated using quantitative risk assess-
ment, a mathematical approach that begins from tox-
icological studies on laboratory animals, sometimes incor-
porating safety factors, to estimate the threshold or safe
dose for each chemical to be regulated. In the case of
cancer, it is generally agreed that no-effect levels are not
likely to exist, so the threshold is calculated as the dose
that poses some level of risk determined a priori to be
acceptable (typically a 10^-5 or 10^-6 additional lifetime risk
of cancer). Based on an array of assumptions about
human behavior and intake, risk assessment is then used
to estimate the level of environmental contamination
that will cause a hypothetical “most exposed individual”
(MEI) not to exceed the acceptable exposure level. With
further assumptions about pollutant fate and transport,
the next step in risk assessment is to calculate the maxi-

mum release rate that will ensure that contamination will
not exceed this level in the vicinity of the facility.

This maximum acceptable release rate becomes the
permitted discharge level, and industries typically
comply with the limit by installing pollution-control
devices or improving housekeeping practices. In rare
cases, more restrictive action than prescribed by a risk
assessment—such as banning a chemical—can be taken,
but only when the evidence from epidemiological or eco-
logical studies is overwhelming that a specific substance
has caused severe health and environmental damage.
Restrictions applied in the 1970s to DDT and the use of
lead compounds in gasoline and paint in many nations
are prime examples.

In principle, the individual elements of the risk para-
digm—prediction of acceptable discharges and expo-
sures, the focus on assessment and regulation of individ-
ual substances on a local scale, and the reliance on pol-
lution control and disposal—are separable. In practice,
however, they usually appear together, because the
system’s risk-assessment methods limit the description of
hazards to those that can be managed using permits and
control technologies. In this way, the elements of the risk
paradigm complement and reinforce each other, creating
a self-consistent system that, through its own lens, is com-
petent to protect health and the environment.

The fact is that the risk paradigm has failed to prevent
global chemical contamination, because the global haz-
ards that synthetic chemicals pose are fundamentally dif-
ferent from the kinds of local, temporary risks for which
this approach was designed. In at least six ways, the
assumptions of the risk paradigm are deeply at odds with
the reality of global toxic pollution. The details of that
reality reveal the extent of and reasons for the failure of
the dominant approach.

**FAILURE 1: ACCUMULATION OF
PERSISTENT POLLUTANTS**

The first problem with the risk paradigm lies in its
assumption that there is an “acceptable” discharge of
synthetic chemicals that will not overwhelm the ecosystem’s
assimilative capacity. Permitting discharges in limited
amounts has often worked effectively for the kinds of non-
synthetic pollution to which this approach was originally
applied—human and animal waste, oil and grease, acids
and bases—because ecosystems can assimilate such sub-
stances, so long as they are introduced at rates below the
degradation or buffering capacity of the system. It has not
been appropriate or effective, however, for the many syn-
thetic pesticides, solvents, refrigerants, chemical feed-
stocks, intermediates, and unintentional byproducts that
are, by design or coincidence, resistant to natural degra-
dation processes. Many of these substances have environ-
mental half-lives measured in years, decades, or centuries
(Table 1). Many more are bioaccumulative—oil-soluble
substances that accumulate in the fatty tissues of living

<table>
<thead>
<tr>
<th>Substance</th>
<th>Half-life (Years)*</th>
<th>Medium</th>
<th>Reference†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon tetrachloride</td>
<td>24.3</td>
<td>Atmosphere</td>
<td>Montzka et al.95</td>
</tr>
<tr>
<td>Dichlorodifluoromethane</td>
<td>69.3</td>
<td>Atmosphere</td>
<td>Montzka et al.95</td>
</tr>
<tr>
<td>Chlorodifluoroethane (HCFC-142b)</td>
<td>13.2</td>
<td>Atmosphere</td>
<td>Montzka et al.95</td>
</tr>
<tr>
<td>Hexachlorobenzene</td>
<td>7</td>
<td>Atmosphere</td>
<td>Cortes et al.96</td>
</tr>
<tr>
<td>Hexachlorocyclohexane</td>
<td>13</td>
<td>Atmosphere</td>
<td>Cortes et al.96</td>
</tr>
<tr>
<td>Chloroform</td>
<td>1,850</td>
<td>Water</td>
<td>Jeffers et al.97</td>
</tr>
<tr>
<td>1,2-Dichloroethane</td>
<td>72</td>
<td>Water</td>
<td>Jeffers et al.97</td>
</tr>
<tr>
<td>Hexachloroethane</td>
<td>1.8 · 10^9</td>
<td>Water</td>
<td>Jeffers et al.97</td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>1.3 · 10^6</td>
<td>Water</td>
<td>Jeffers et al.97</td>
</tr>
<tr>
<td>perchloroethylene</td>
<td>990 · 10^6</td>
<td>Water</td>
<td>Jeffers et al.97</td>
</tr>
</tbody>
</table>

*Atmospheric half-lives are derived from actual environmental measurements; aquatic half-lives from hydrolysis constants in
pure water.
†For complete reference citations, see the reference list.
things and multiply in concentration as they move up the food chain (Table 2). Some bioaccumulative substances reach concentrations in upper trophic wildlife, including humans, that are tens of millions of times greater than their levels in the ambient environment.6,7

Because of their tendency to build up rather than break down, releases of persistent and/or bioaccumulative substances since the expansion of synthetic chemical manufacturing after World War II have resulted in the global accumulation of a large number of POPs. These chemicals are distributed long distances on currents of wind and water and have therefore accumulated, sometimes in very high levels, in the ambient environment and food web in areas remote from any known sources of these substances, including the high Arctic,8,10 the isolated rainforests of South America and Africa,11 and the deep and open oceans.6,12 In the Arctic, where long residence times, cold temperatures, and long food chains combine to enhance the persistence and bioaccumulation of organic chemicals, body burdens of humans and wildlife are as much as an order of magnitude greater than they are in industrialized regions at temperate latitudes.13,14

Although research and policy have focused primarily on a handful of substances—PCBs, dioxin, and about a dozen organochlorine pesticides, global contamination cannot be reduced to a few “bad actors.” In the Great Lakes, 362 synthetic chemicals have been “unequivocally identified” in the water, sediments, and food chain; the list includes the most infamous organochlorines, but it also contains a full spectrum of less familiar substances, from simple solvents to a host of complex industrial chemicals and byproducts.15 Polychlorinated terphenyls are widespread in the water, sediment, and biota of Northern Europe,16 and pesticides presumed to be relatively non-persistent— atrazine, chlorpyrifos, endosulfan, chlorothalonil, metolachlor, and terbufos—can now be measured in Arctic air, water, and fog.10 Industrial byproducts, including chloroanisoles, chloroveratroles, and octachlorostyrene, are present in measurable quantities in the Canadian Arctic10 and over the remote Atlantic ocean,17 and a variety of chlorinated benzenes are ubiquitous components of rain and snow.18 Atrazine, alachlor, and chlorpyrifos are widespread in air, fog, groundwater, and surface water throughout large parts of North America, even in areas remote from the places where they are used.19,20 And halogenated solvents, refrigerants, and their haloacetate breakdown products have become truly ubiquitous contaminants of the troposphere, stratosphere, and vegetation.21-23

With the environment and food web ubiquitously contaminated, it should come as no surprise that the bodies of human beings are, as well. An estimated 700 xenobiotic organic chemicals are present in the adipose tissues of the general population of the United States.24 At least 188 organochlorine pesticides, solvents, plastic feedstocks, specialty chemicals, byproducts, and metabolites have been specifically identified in the blood, fat, milk, semen, urine, and/or breath of the general U.S. and Canadian population—people with no special workplace or local exposures to these substances (Table 3). For bioaccumulative substances, the vast majority of the average individual’s exposure—in excess of 90%—comes through the food supply, primarily from animal products.25 For some of the best-studied substances, the general public’s average body burden is already at or near the ranges at which health impacts have been documented in laboratory animals.25-27

The now-ubiquitous global presence of myriad synthetic chemicals, in large-scale production for just over half a century, supports a simple inference: substances that persist or bioaccumulate cannot be integrated into natural cycles. Discharged in even very small amounts,

### Table 2: Bioconcentration Potentials of Selected Synthetic Chemicals

<table>
<thead>
<tr>
<th>Substance*</th>
<th>Fat Solubility† (Kow)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrazine</td>
<td>407</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>676</td>
</tr>
<tr>
<td>Perchloroethylene</td>
<td>2,512</td>
</tr>
<tr>
<td>Monochlorobenzene</td>
<td>3,802</td>
</tr>
<tr>
<td>Trichlorophenols</td>
<td>4,989-18,621</td>
</tr>
<tr>
<td>g-Hexachlorocyclohexane</td>
<td>5,348</td>
</tr>
<tr>
<td>Endosulfan</td>
<td>6,761</td>
</tr>
<tr>
<td>Hexachlorocyclopentadiene</td>
<td>9,772</td>
</tr>
<tr>
<td>Trichlorobenzenes</td>
<td>10,471-15,488</td>
</tr>
<tr>
<td>Tetrachlorobenzenes</td>
<td>50,119</td>
</tr>
<tr>
<td>Hexachlorobutadiene</td>
<td>79,433</td>
</tr>
<tr>
<td>Pentachlorobenzenes</td>
<td>147,911</td>
</tr>
<tr>
<td>Hexachlorobenzene*</td>
<td>1,949,845</td>
</tr>
<tr>
<td>Tetrachlorodibenzofurans*</td>
<td>660,693</td>
</tr>
<tr>
<td>Octachlorostyrene</td>
<td>1,949,845</td>
</tr>
<tr>
<td>Tetrachlorodibenzo-p-dioxin*</td>
<td>6,309,573</td>
</tr>
</tbody>
</table>

*Of these substances only three (*) are addressed in the draft global agreement on POPs.
†Expressed as the octanol–water coefficient.
Data source: National Library of Medicine.98

### Table 3: Synthetic Organochlorines Detected in the Adipose Tissue, Blood, Milk, Breath, and/or Urine of the General Human Population of the United States and Canada

<table>
<thead>
<tr>
<th>Substance Class</th>
<th>Substances Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloromethanes</td>
<td>12</td>
</tr>
<tr>
<td>Chloroethanes</td>
<td>9</td>
</tr>
<tr>
<td>Chloroethylenes</td>
<td>3</td>
</tr>
<tr>
<td>Other chloroaliphatics</td>
<td>10</td>
</tr>
<tr>
<td>Chlorobenzenes</td>
<td>12</td>
</tr>
<tr>
<td>Chlorophenols</td>
<td>3</td>
</tr>
<tr>
<td>Chlorodiphenyl ethers</td>
<td>6</td>
</tr>
<tr>
<td>PCBs</td>
<td>86</td>
</tr>
<tr>
<td>Polychlorinated dibenzodioxins</td>
<td>8</td>
</tr>
<tr>
<td>Polychlorinated dibenzofurans</td>
<td>10</td>
</tr>
<tr>
<td>Other chlorinated aromatics</td>
<td>8</td>
</tr>
<tr>
<td>Pesticides</td>
<td>21</td>
</tr>
</tbody>
</table>

Source: Thornton.1
these chemicals build up gradually in the environment and in living things. Given enough time, even very small “acceptable” discharges ultimately reach unacceptable levels. The ecosystem’s assimilative capacity for persistent or bioaccumulative substances is therefore zero, and the only “acceptable” discharge is also zero. Any amount greater than zero must be expected to lead to some degree of long-term, global contamination.

**FAILURE 2: CUMULATIVE GLOBAL POLLUTION**

The second problem with the current approach to chemical pollution is that the focus on individual facilities and the local environments around them is fundamentally at odds with the global, cumulative nature of chemical pollution. When a facility is granted a permit to discharge pollutants into the air or water (or when the regulations that provide the guidance for these permits are formulated), the risk assessments on which these decisions are based consider only local and immediate exposures through one or a few exposure routes. The central construct of a risk assessment is a “most exposed individual” (MEI), a hypothetical person who suffers very high local exposures. In the simple case of an air-emissions permit, for example, the MEI stands at the edge of the facility grounds, breathing deeply, 24 hours a day for 20 years or more. The risk assessor uses data and assumptions about the height of the smokestack, the direction and speed of the wind, the amount of air a person breathes, and the toxicity of each substance to “back-calculate” a maximum permissible emission rate.

By this method, any quantity of the pollutant not ingested by the most exposed individual simply disappears. These dispersed and ignored emissions in fact represent the vast majority of pollutant releases, since no MEI takes into his or her body more than a tiny fraction of the chemicals released from the facility. In the risk paradigm, whatever quantity of a pollutant is taken up by wind or water currents and transported long distances is of no consequence. If a facility builds a higher smokestack or a longer discharge pipe, ensuring that emissions will be diluted in the air or water, then risks to the MEI will be reduced, and larger quantities of pollutants can be permitted. In this way, risk-based discharge permits allow—and even encourage—global pollution.

Moreover, when the risk paradigm assesses and permits releases of a chemical from a single facility, it takes no account of the fact that there may be hundreds of other facilities emitting the same chemical, in the same region or around the world. There are thousands of individual sources permitted to release thousands of pollutants. Even if releases from each of these facilities are locally acceptable, their emissions are dispersed together across the planet, contributing to a total chemical load that the local view never even considered. Preventing even extreme local contamination from myriad individual facilities, each permitted to operate simultaneously, year after year, does nothing to prevent the slow accumulation of a global pollution burden.

The problem is not only with facility-based permitting but also with risk assessment as a mode of hazard evaluation. There is no accepted method to evaluate the impacts of individual or multiple pollution sources in the context of the total, worldwide exposure burden. By relying on a model that pollutants travel directly and predictably from their discharge point to a single most exposed individual or local ecosystem, risk assessment as currently practiced and applied inherently precludes consideration of the global effects of the entire universe of pollution sources.

**FAILURE 3: TOXICOLOGICAL COMPLEXITY**

The third reason that the risk paradigm is inadequate to prevent global pollution is that the complex biological impacts of chemical mixtures cannot be adequately predicted or prevented with assessments and management strategies that focus on individual substances. There are 70,000 synthetic chemicals in commerce, and, as we have seen, many hundreds have already accumulated in the bodies of the human population. In the current policy framework, each chemical is assessed and regulated individually. Acceptable discharge and exposure levels for each substance are extrapolated from laboratory studies using a classic reductive approach to reveal causality: animals are exposed to varying doses of a single pollutant, and the effect of that pollutant can be clearly discerned because all other factors are held constant. The assumption is that assessments of the toxicity of a substance at a given dose level will also hold when exposure occurs in the context of a chemical mixture.

This assumption has been resoundingly falsified by repeated findings that pollutants interact to modulate each other’s toxicity in surprising and extreme ways. Although additive and inhibitive interactions occur, the most common effect of binary mixtures is a multiplicative or exponential effect by which the whole is greater than the sum of its parts. The pesticide fenarimol, for example, greatly increases the mutagenicity of trichloroethylene, and trichloropropene oxide and dioxins both amplify the carcinogenicity of certain polyaromatic hydrocarbons. The magnitude of the synergistic effect can be extreme: exposure to a usually nontoxic dose of the pesticide chlordecone increases the death rate 67-fold among rats exposed to an “otherwise inconsequential” dose of carbon tetrachloride. When a dose of PCBs that causes a 1.5-fold increase in liver porphyrin levels in rats is combined with a dose of dioxin that in isolation causes no measurable porphyrin elevation, porphyrin levels increase by 650 times.

Single-chemical predictions of toxicity are therefore not reliable, and exposures predicted to be safe based on risk assessment may cause considerable health damage.
In a classic study, rats exposed to a mixture of 25 common groundwater pollutants, all at levels well below the doses that produce any measurable effects in isolation, exhibited statistically significant immunosuppression and increased susceptibility to several kinds of infectious diseases. When this same mixture was applied along with ionizing radiation, it substantially amplified the toxicological potency of radiation to rat bone marrow. Indicating that it is not only chemicals that interact with each other but biologically active agents of entirely different classes.

The real-world impacts of chemical pollution therefore cannot be predicted with confidence based on single-chemical assessments. Even the use of comparative risk assessment to prepare priority lists of individual chemicals fails to take account of the true modes by which chemicals disrupt biological systems. It is the total chemical burden—the complete set of environmental hazards of all types, in fact—that poses potential health hazards; single-chemical studies, conducted completely out of this context, offer little insight into the hazards that the components of these mixtures actually pose. Single-chemical studies clearly have scientific value: with their simplified exposure regimens, these experiments are indispensable for clarifying the mechanisms by which individual components evoke their toxic effects. But value for science is not the same as value for policy, and the inescapable conclusion is that discharges or exposures cannot be approved based on risk assessment with confidence that health will not be damaged.

This problem is intrinsic to the risk-based approach. One might reasonably suggest that toxicological testing and risk-assessment methods should focus on the effects of individual chemicals in the context of chemical mixtures. But evaluating the role of each individual compound in a mixture and its interactions with all the others would require a multifactorial design that examines all possible combinations of the chemicals. Such studies are astronomically demanding of time and resources. According to scientists at the National Toxicology Program, an abbreviated single-species, 13-week toxicity evaluation of all the interactions in a mixture of just 25 chemicals would require over 33 million experiments at a cost of about 3 trillion dollars. A similar study of just 1% of the chemicals in commerce would require an unimaginable $10^{30}$ experiments.

In practice, gaining insight into the effects of chemical mixture does not really require probing the roles of individual substances in all possible combinations. It is much more practical and revealing to pluck a real-world mixture of chemicals from some corner of the environment and compare the effects it causes with those of a mixture from some less-contaminated place. For example, several studies have compared the health of animals fed fish from large contaminated ecosystems such as the Great Lakes or the Baltic Sea with the health of those fed fish from less contaminated environments, and they have found that the chemical mixtures in fish have adverse effects on immunity, reproduction, and behavior. But these studies do not indicate which compounds in the mixture are causing the effects, so their results become irrelevant and inadmissible when decisions are required to focus on single chemicals. We do not lack evidence that the low-level chemical mixtures present in the environment can cause health damage; rather, the problem is that the current regulatory system is blind to data that cannot be reduced to a simple cause–effect, single-chemical model.

**FAILURE 4: INADEQUATE DATA**

The fourth problem with risk-based regulations on individual substances is that the data to support them simply do not exist. According to a 1984 National Research Council report, data for a complete health-hazard assessment were not available for a single industrial chemical, and there were no data whatsoever for 78%. A 1997 update of that study found that the situation had not improved: even among the subset of high-volume chemicals that had already been the subject of specific regulatory attention—those expected to have been the most thoroughly studied—70% still lacked even minimal chronic toxicity data; no reproductive toxicity tests were available for 53%, no neurotoxicity information for 67%, and no immunotoxicity data for a whopping 86%. As for the thousands of additional substances formed as byproducts, environmental transformation products, or metabolites, toxicological data are likely to be even less ample for these substances than for those that are officially on the market.

New toxicological data can be obtained, but we cannot hope to amass the information base to effectively regulate synthetic substances individually any time soon. The U.S. National toxicology program conducts assessments for 10 to 20 substances per year, but the chemical industry brings 500 to 1,000 new chemicals into commerce annually. Our knowledge base is constantly falling further and further behind the diversity of chemicals introduced into the environment.

This lack of data fundamentally undermines the ability of the risk paradigm to protect health. In the current system, synthetic chemicals are presumed harmless until demonstrated hazardous. In a risk assessment, a chemical for which there are no toxicological data is assigned a risk of zero, and a substance with a zero risk is subject to no restrictions whatsoever. The result is that the current system operates primarily on ignorance rather than knowledge, and the vast majority of chemicals receive laissez-faire treatment simply because they have been studied superficially, if at all. Predictions that the public’s exposures are safe have no empirical basis in observation or even extrapolation. Chemicals are often left off priority lists not because they are less hazardous than other substances but because we know little or nothing about them.
The question is, how severe are the hazards we have not yet detected? At the time of their introduction in the late 1920s, chlorofluorocarbons were considered absolutely safe; some 50 years later, they were found to cause severe damage to the stratospheric ozone layer.45 More recently, tris(4-chlorophenyl)methanol (TCM), an exotic industrial specialty chemical and by-product that had not been the subject of previous scientific or regulatory attention, was sought and found at levels up to the parts per million in wildlife tissues on a truly global basis; toxicological evaluations have just begun, and TCM has been found to be an estrogen receptor agonist, raising the possibility of a variety of reproductive, developmental, behavioral, and pathological impacts. It remains unknown how many other chemicals with the potential to cause severe health damage are globally distributed but presently unrecognized.

**FAILURE 5: FORMATION OF CHEMICAL MIXTURES**

Even if it were possible to develop data and regulations for each individual organochlorine, chemical-by-chemical regulations and assessments would still fail to address the ways that that synthetic chemicals are produced—always in complex mixtures, many of the components of which are unidentified. Over 300 organochlorine byproducts have been identified, for example, in the effluents of chlorine-bleaching pulp mills, including a tremendous diversity of chemical structures: chlorinated dioxins, furans, phenols, benzenes, thiophenes, methylsulfones, methanes, ethanes, acids, and PCBs.48,49 The identified substances account for only 3 to 10% of all the organically-bound chlorine in the effluent; the remaining 90 to 97% have not been chemically identified or assessed.50 Similarly, the emissions of waste incinerators are estimated to contain over 1,000 products of incomplete combustion,51 including a wide range of chemical structures, from carbon tetrachloride to chloronaphthalenes and dioxins.52-55 The most ambitious studies have identified just 40 to 60% of the total mass of unburned hydrocarbons in the stack gas.54,55 In the disinfection of water with chlorine gas, scores of byproducts have been identified, ranging from chloromethanes to chlorophenoxophenols and chlorodibenzofurans,56-59 and unidentified compounds represent 50 to 75% of the total organically-bound chlorine in the water.59,60

Even in more carefully controlled chemical synthesis processes, mixtures are always produced. Byproducts account for almost 20% of commercial DDT preparations, and about one sixth of this is unidentified compounds.62 All lesser chlorinated benzenes are contaminated with considerable quantities of the highly persistent and bioaccumulative hexachlorobenzene, because the chlorination of benzene inevitably proceeds, in part, to the saturated form.63 In the production of short-chain chlorinated hydrocarbons by chlorinolysis, 1% to 7% of the total yield consists of highly persistent and bioaccumulative organochlorine byproducts.63 And in the reactions by which vinyl chloride is synthesized, 10% of the yield consists of organic byproducts including the very hazardous hexachlorobenzene, hexachlorobutadiene, hexachloroethane, PCBs, dioxins, and furans; the wastes from this process are over 60% chlorine by weight, and about 30% of the contents are unknown compounds.64-65

If synthetic chemicals are always produced in diverse mixtures, it is unrealistic to think we can regulate and control them individually. Even trying to assess these substances on a chemical-by-chemical basis fails to provide the kind of knowledge necessary to make effective policy; an assessment that considers only the fate and toxicity of a commercial chemical—and excludes all the byproducts formed in its manufacture, use, and disposal—may radically underestimate the actual health and environmental damage that a substance may cause. Moreover, managing chemicals on a substance-by-substance basis requires us to know what chemicals we are producing. In fact, we do not even know the chemical names or structures of the majority of the byproducts formed in industrial processes, not to mention their toxicity and environmental behavior. We cannot assess and control substances that have not even been identified, so our blindness to the composition of the mixtures produced in chemical-intensive industrial processes fundamentally undermines the chemical-by-chemical approach to environmental regulation.

Suppose society decided to eliminate just a few of the most persistent, toxic, and bioaccumulative substances, such as those on UNEP’s list of 12 POPs. Policies targeted specifically at a short list of chemicals would still have to address the production and disposal of entire classes of compounds and technologies, because of the formation of unintentional mixtures. The continuing discharge of tons of PCBs into the environment each year as byproducts of chlorine-based industrial processes, decades after the deliberate production of PCBs was phased out, for example, clearly illustrates this problem.66 Perhaps the greatest challenge comes from 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), the most persistent, bioaccumulative, and toxic of all synthetic chemicals known. TCDD and/or related compounds have been detected as byproducts in the electrolytic production of chlorine gas; in all direct applications of chlorine; in the manufacture of any and all chlorinated organic chemicals, including plastic feedstocks, solvents, pesticides, intermediates, and specialty chemicals; in some uses of chlorine-based substances; and in the purposeful or accidental combustion of any and all organochlorines (Table 4). The conclusion is that dioxin formation appears to be endemic to the industrial use of chlorine chemistry. No organochlorine can go through its life cycle of manufacture, use, and disposal without producing dioxin along the way. If we want to stop the production of the single most hazardous substance, it is nec-
necessary to address the entire class of industrial substances and technologies derived from the use of chlorine gas and organochlorine compounds.

**FAILURE 6: POLLUTION CONTROL AND DISPOSAL**

The final reason that the risk paradigm has failed is that the technological effort to control pollutants rather than prevent their generation inevitably leads to global accumulation. Devices for pollution control and disposal can help a facility to meet discharge limits and thereby reduce local contamination, so they have become the technological centerpiece of the risk paradigm. But these technologies do little or nothing to prevent global pollution. The predominant effect of control and disposal devices is to shift chemicals from one environmental medium or chemical form to another. The most effective precipitators, scrubbers, filters, evaporation tanks, and landfill liners merely change the time or place in which persistent pollutants enter the environment; immediately or eventually, captured pollutants make their way into the ecosystem in one place or another, in one form or another.

As for incinerators, these devices not only shift pollutants from one medium to another but convert them to new forms; the desired products are carbon dioxide and water, but even properly operated facilities convert a considerable portion of the wastes they burn into persistent and toxic products of incomplete combustion (PICs). PICs are the inevitable result of the random combustion reactions and post-combustion processes; improved operating conditions can reduce their formation but cannot prevent them. Further, metallic pollutants such as lead, mercury, and cadmium cannot be destroyed by burning at all, and incinerators serve simply as dispersion points for these pollutants. Ironically, it is incinerators—the centerpiece of the pollution-control infrastructures in most industrialized countries—that are the largest identified sources of dioxin and leading sources of many metallic pollutants.

Pollution-control strategies are further undermined by the fact that many chemicals, such as pesticides, paint

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**TABLE 4 Selected Industrial Processes in Which the Generation of Polychlorinated Dibenzo-p-dioxins or Related Compounds Has Been Identified**

<table>
<thead>
<tr>
<th>Category</th>
<th>Dioxin-generating Process</th>
<th>Reference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production of chlorine gas</td>
<td>Chlor-alkali with graphite electrodes</td>
<td>Rappe et al.99</td>
</tr>
<tr>
<td></td>
<td>Chlor-alkali with titanium electrodes</td>
<td>Environment Agency64</td>
</tr>
<tr>
<td>Direct chloride applications</td>
<td>Pulp bleaching</td>
<td>U.S. EPA68</td>
</tr>
<tr>
<td></td>
<td>Water treatment</td>
<td>Rappe et al.57</td>
</tr>
<tr>
<td></td>
<td>Metallurgy</td>
<td>Oehme et al.100</td>
</tr>
<tr>
<td></td>
<td>Production of inorganic chlorides</td>
<td>Hutzinger and Fiedler101</td>
</tr>
<tr>
<td>Synthesis of organochlorines</td>
<td>All chloroaromatics (pesticides, intermediates, specialty chemicals)</td>
<td>Environment Agency,64 Heindl and Hutzinger102</td>
</tr>
<tr>
<td></td>
<td>Chlorinated solvents</td>
<td>Environment Agency,64 Heindl and Hutzinger102</td>
</tr>
<tr>
<td></td>
<td>Aliphatic plastic feedstocks</td>
<td>Hutzinger and Fiedler101</td>
</tr>
<tr>
<td>Uses of organochlorines</td>
<td>Synthesis with organochlorine intermediates</td>
<td>Hutzinger and Fiedler101</td>
</tr>
<tr>
<td></td>
<td>Solvent use in alkaline environment</td>
<td>Rappe and Marklund103</td>
</tr>
<tr>
<td></td>
<td>Lumber treatment with pentachlorophenol</td>
<td>Marklund et al.104</td>
</tr>
<tr>
<td>Disposal of organochlorines</td>
<td>Waste combustors</td>
<td>U.S. EPA68</td>
</tr>
<tr>
<td></td>
<td>Copper-recycling smelters</td>
<td>U.S. EPA68</td>
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<tr>
<td></td>
<td>Ferrous metal smelters</td>
<td>U.S. EPA68</td>
</tr>
<tr>
<td></td>
<td>Open-barrel waste combustion</td>
<td>U.S. EPA68</td>
</tr>
<tr>
<td>Accidental combustion of organochlorines</td>
<td>Building fires with PVC plastic</td>
<td>U.S. EPA68</td>
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<tr>
<td></td>
<td>Vehicle fires with PVC plastic</td>
<td>U.S. EPA68</td>
</tr>
<tr>
<td></td>
<td>Landfill and warehouse fires</td>
<td>U.S. EPA68</td>
</tr>
<tr>
<td>Environmental transformation of organochlorines</td>
<td>Transformation of substances in sewage sludge</td>
<td>Oberg et al.105</td>
</tr>
<tr>
<td></td>
<td>Photolytic transformation of airborne chlorophenols</td>
<td>Baker and Hites106</td>
</tr>
</tbody>
</table>

*For complete reference citations, see the reference list.
strippers, and plastics, are deliberately dissipated into the environment or the economy. When the goal is to prevent local contamination, dissipation of this sort is of little consequence, but it contributes considerably to global contamination. Once a pesticide is sprayed onto agricultural land, a paint stripper sold to a handyman, or PVC pipes installed in a building that may one day catch fire and thus generate dioxins, even the most efficient devices attached to factories become irrelevant. In these cases, the hazard comes from the product, not a waste, and the only way to prevent the release of these substances or their ultimate byproducts into the environment is not to produce and use them at all.

Further, control and disposal technologies seldom perform as well in reality as they are supposed to. Human error, aging equipment, and fluctuations in operating and environmental conditions can all result in unexpectedly large releases of chemicals to the environment during capture or disposal. Landfill liners decay and leak, incinerators undergo upset conditions and explosions, chemicals are spilled, and so on. With the use of synthetic products expanding globally, especially in developing countries where regulatory and technological infrastructures are less developed, the scenario of optimally designed, operated, supervised, and maintained control and disposal technologies becomes highly unrealistic.

Finally, the goal of pollution control is to reduce the quantity of emissions per unit product, economic growth in the rate of production eventually overwhelms improvements in the rate of emissions per unit product. In theory, perpetual increases in pollution-control efficiency could avoid this problem. In reality, however, after an initial reduction in discharges, the cost of improved control increases exponentially, so it quickly becomes prohibitively expensive to achieve further reductions, and companies must spend more and more on control just to maintain a constant rate of environmental pollution.

**BEYOND RISK**

These six issues show why the current system for chemical assessment and regulation is intrinsically ill-suited to preventing global pollution. At the heart of the risk paradigm’s failure is an inappropriate model of nature on which risk assessment and its pretense of predictive management of environmental hazards are based. Quantitative risk assessment was adapted from the methods used by engineers and economists to predict the probability that a bridge will collapse or an investment fail. These predictions are reasonably reliable, because the system has been built by humans and is thus well characterized, and only a limited number of factors affect the integrity of the bridge. The system is classically mechanical and linear: the effect of weakness in one part of the bridge on another part is well understood, and the probabilities of individual events can be added or multiplied to yield the probability of an overall outcome. Although there are always uncertainties, these too can be defined and even quantified. Finally, the impacts of failure are local and immediate, and each risk can be considered in isolation, since the collapse of a bridge at one location has no effect on the integrity of a bridge elsewhere. The same model underlies environmental risk assessment’s attempt to quantify the risks of specific forms of health damage caused by individual chemicals.

This mechanical, probabilistic model is inappropriate for ecosystems and organisms, which are not built objects but are alive, unpredictable, densely interconnected, hierarchical, and largely uncharacterized complex systems. In systems such as this, quantitative predictions are unreliable. The first barrier to reliable prediction is missing data; when the initial values that should be put into a predictive model are not known, we can have no confidence whatsoever in the output.

Second, we cannot predict the impacts of perturbing a system unless the system itself is well characterized, but knowledge of the specific fundamental mechanisms (at molecular, cellular, organismal, population, and community levels) by which organisms and ecosystems develop and function remains partial at best. For example, new molecular components of the vertebrate endocrine system are continually discovered, and the physiological functions of many potential hormone receptors remain unknown. The dynamics of relationships among species in an ecosystem also remain largely uncharacterized. Without relatively complete knowledge of how organisms and ecosystems function, there is no way we can reliably predict or manage the effects of the multiple, simultaneous changes we inflict upon these systems.

Finally, prediction works well in simple physical systems with determinate, linear paths of causality: that is, each cause produces one effect, and the total result of numerous small causes is simply the sum of all their individual impacts. Organisms and ecosystems, in contrast, are characterized by multifactorial and circular causality—negative and positive feedback loops, redundancy, multiple functions, critical periods of high sensitivity, and so on. Circular webs of causality mean that the system is buffered against some changes, but it is extremely sensitive to others. Multiple tiny changes can cause runaway or synergistic effects, resulting in a major reorganization or breakdown of the system. Other impacts may be more subtle, degrading the performance or adaptability of the system without the obvious signs of failure. The ability of tiny, one-time doses of endocrine-disrupting chemicals during early development to cause delayed multigenerational damage to reproductive and cognitive function is powerful testament to this dynamic.

The impossibility of making reliable quantitative predictions of the impacts of individual substances on ecosystems and organisms falsifies the risk paradigm’s most basic assumption: that humans have the knowledge and technology to manage these impacts at the fine level of control implied by approving discharges and regulat-
First and foremost, the ecological paradigm recognizes the limits of science, which provides important clues about nature but can never completely predict or diagnose the impacts of individual chemicals on natural systems. The implications for policy are obvious: since science leaves so much unknown, we cannot afford to make risky bets on its predictions or wait to protect health and the environment until we have proof of specific causal links. Instead, we should avoid practices that have the potential to cause severe damage, even in the absence of proof. This perspective embodies the principle of precautionary action in the face of scientific uncertainty: when the potential impacts of a mistake are severe and irreversible, we should err on the side of caution by anticipating and preventing environmental damage.

Precaution implies that substances and technologies that may be reasonably presumed to pose hazards should be avoided, whether or not scientists can prove that damage has already been done.

The precautionary principle tells us not to wait for proof before taking action, but it does not specify what kind of action to take, so the ecological paradigm relies on four other principles, which are formulated specifically to address the limits of the risk paradigm.

- First is the principle of zero discharge: to prevent the accumulation of persistent and bioaccumulative substances, these chemicals are considered incompatible with ecological processes, and releases in any quantity are considered a potential hazard. The goal of policy becomes not the licensing of “acceptable” discharges but eliminating releases of such substances altogether.
- To accomplish this goal, the ecological paradigm takes a new technological approach with clean production. In contrast to the after-the-fact strategy of pollution control and disposal, clean production emphasizes front-end solutions, particularly the redesign of products and processes to eliminate the use and generation of toxic chemicals, before they need to be managed. For example, a clean production approach to emissions of the solvent perchloroethylene from dry cleaners replaces the old process with a new generation of machines that use water, steam, or liquid carbon dioxide to clean clothes. The principle of clean production says simply that we should always use the cleanest available technology to fulfill society’s needs. Assessment of alternatives rather than approval of pollution becomes the centerpiece of environmental management.
- To address the overwhelming lack of information that undermines the chemical-by-chemical approach, the ecological paradigm shifts the burden of proof, an idea called “reverse onus.” In the current system, chemicals are presumed to be harmless until demonstrated hazardous. As a result, a lack of data is misconstrued as evidence of safety, and all the untested and unidentified chemicals are assumed to be safe. In
the ecological paradigm, the burden of proof shifts to those wanting to produce or use a synthetic chemical, who must demonstrate in advance that their actions are not likely to pose a significant hazard and that there is no safer alternative available. This is the same standard that is supposed to be applied to pharmaceuticals in the United States before they are brought to the market, and there is no reason chemicals that enter our bodies indirectly and involuntarily via the environment should be subject to any less scrutiny.

- Finally, to cope with the impossibility of micromanaging the diversity of hazards produced by modern technologies, the scale of preventive measures in the ecological paradigm shifts from micromanagement of individual sources and substances to large classes of chemicals and the processes that produce them. Priority in environmental policy is given to those classes whose members tend to have the most hazardous qualities. Organohalogen and metallic pollutants are obvious choices for immediate action.

Based on these principles, the ecologic paradigm would require progressive reductions in the use of all synthetic chemicals—a gradual process to transform current industrial technology, with its countless individual hazards, into an economic base that is compatible with ecological processes. It is clear that safer alternatives exist already for most applications of POPs; although many require investment, they are economically and technically feasible.1,85,86

Implementation of the ecological paradigm involves a carefully planned process called “chemical sunsetting.”787 Sunsetting begins by reversing the onus for classes of chemicals and processes for which a prima facie case can be established that their members may be hazardous; members of these classes are treated as candidates for phase-out, and specific exceptions are made for uses that can be demonstrated non-hazardous to a reasonable degree of certainty or to fulfill an important need for which no alternative is available. The goal of environmental policy becomes zero discharge of these substances, and progress is made towards that goal by converting the sources of priority substances to cleaner materials and technologies.

Because the problem is global, the policy should be implemented on an international scale. And because persistent synthetic chemicals are used in a wide variety of industrial processes, the complete conversion to safer technologies will take decades. Chemical sunsets require priorities and timelines to be established, exceptions to be granted, and the safest and most effective substitutes to be chosen; these decisions should be made democratically and be specifically tailored to each nation or region, preferably through a transition planning board that is representative in its makeup and held accountable to the public at all stages of the process.

Some critics have argued that treating classes of substances from a precautionary perspective is radical and unscientific.88,89 But in making public policy decisions, society always chooses the appropriate level of intervention. We do not try to address insect infestations by targeting individual bugs or traffic problems by regulating individual cars. In these cases, society has decided that it is more effective to focus on systemic causes rather than their individual manifestations, which are too numerous and dispersed to be micromanaged. Ozone-depleting compounds, PCBs, and lead compounds all represent chemical classes whose members have been addressed as together, based on a recognition of their common sources or their contributions to a common problem. Addressing all synthetic chemicals according to their broad classes would extend this precedent to a much larger group of substances. There are thousands of members of the class of organohalogen, for example: although most have not been well studied, virtually all of those that have been tested have turned out to be hazardous,1,90 often at extremely low doses, and their hazardous qualities can be understood as the expected outcome of the impacts at the molecular level of halogenating organic substances.1,91 For diverse and generally hazardous classes of chemicals such as this, macromanagement is well justified.

TOWARD GLOBAL ACTION

Although the risk paradigm dominates contemporary environmental policy, alternative approaches have been used in various times and places. Indeed, aspects of the ecological paradigm have been implemented on an ad-hoc basis, and these actions have been far more successful at reducing global pollution than risk-based regulations. For example, restrictions in many nations on the production and use of such pollutants as DDT, PCBs, and CFCs, and major uses of lead and mercury have led to drastic reductions in releases of these compounds, and environmental levels and human exposures have gradually followed suit. In contrast, permit and control regulations during the 1970s and 1980s yielded little or no decrease in the environmental concentrations of numerous major pollutants in the United States.92

More recently, the Swedish Government has instituted the Chemicals Action Programme,93,94 which will phase out several dozen of the most hazardous solvents, pesticides, and bleaching agents. This program effectively implements the principles of clean production and zero discharge by changing the inputs of materials into such processes as agriculture, industrial cleaning and coating, and pulp bleaching. But because it focuses on a relative short list of individual substances, the Chemicals Action Program still addresses only a small fraction of the thousands of chemicals that pose potential health and environmental hazards. Moreover, for all its virtues, the program is national and cannot address the global distribution of POPs and their sources.

The most critical development in the present period is
unquestionably the negotiation of the POPs agreement, now in its final stages under the auspices of the United Nations Environmental Program. Because this instrument represents the first international action to stop the accumulation of persistent toxic substances in the global environment, it represents a significant step forward beyond the local and national efforts of the present. As currently conceived, however, the agreement is not nearly adequate to its task. First, it is unclear whether it will require releases of POPs—particularly those that are produced as accidental byproducts—to be eliminated at the source or simply reduced under a risk-based pollution-control approach. Further, the agreement addresses only 12 “priority” pollutants, and provisions for adding more chemicals to the list of targets at a future date are also a matter of controversy.

As I have shown here, the POPs treaty will effectively address global pollution only if it moves decisively away from the risk-based strategy of prediction, reduction, and control of single chemicals toward a preventive approach focused on converting industrial production systems to eliminate hazardous classes of chemicals entirely. There is no doubt that the very existence of an international instrument to confront toxic pollution on a global scale is a major step forward. The challenge now is to establish a conceptual and legal framework that can effectively and promptly address the thousands of hazardous substances not slated for action in the initial agreement.

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Announcement

The Collegium Ramazzini celebrated the 300th anniversary of the publication of Ramazzini’s *De Morbis Artificum Diatriba* at its annual meeting in Carpi, Italy, on October 27–29, 2000. The celebration was followed by meetings discussing “Present Priorities in Occupational Carcinogenesis.”

The Ramazzini Award, occupational medicine’s most prestigious recognition, was presented by the Collegium Ramazzini to Dr. Eula Bingham, of the University of Cincinnati. Dr. Bingham presented the Ramazzini Lecture, “The Regulation of Carcinogens: The History and the Future.”