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## Addressing plastic additives

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### Headlines

#### Issues

- Hundreds of chemicals with known toxicity to humans and the environment are still widely used as additives in plastics.
- The average consumer's knowledge of what goes into plastic products is not sufficient to make informed choices about exposure. The data collection needed to make these choices often does not exist, especially for recycled products made of mixtures of existing plastics.
- Though data on the toxicology of single additives in isolation may be available, there is very little data on the interaction of multiple additives in real world situations, either within a single product or between many products in a single place.
- Most substances are not restricted until proven toxic. As a result, damage comes first and action second.
- Substance-by-substance testing often results in the substitution of one hazardous molecule by another with similar toxicology.

#### Solutions

- Governments and consumers should demand the use of non-toxic chemicals for use in plastics, especially given the risk of admixture of toxic substances in recycled plastic products.
- Consumers and producers should demand full supply chain transparency on additive presence in plastic products.
- Understanding the toxicology of mixtures of additives requires the generation of substantial new datasets. This data should include biomonitoring to characterise the complexity of real-world exposures.
- Assessments of toxicity should not assume that a low dose always means a low risk.
- Hazardous substances should be regulated by group rather than one-by-one, to avoid substituting one harmful chemical for another.
- A molecular science and engineering approach is crucial to finding chemical and functional alternatives to toxic additives, and also for developing new processes to better manage the toxicity of additives which cannot be replaced or omitted.

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## Objectives

A wide range of chemicals are added to plastics to give them specific desirable characteristics, for example to make them more flexible, give them different colours, increase their resistance to UV radiation or reduce their flammability. However within each of these classes of additives, there are several groups which have been shown to be potentially or actually toxic to human health and the environment. These may be partially released during the production, use, recycling or disposal of plastics.

In this Briefing Topic, we will review the current state of knowledge in the field of plastic additives, their potential toxicity and associated management challenges. We discuss options to address the complications of the current management regime and the sheer variety of substances to be evaluated. We outline how, in order to safeguard future human and environmental health, it is necessary to understand toxicological patterns and develop functional alternatives that do not result in new toxic materials.

## Introduction

### Chemical additives present in humans and the environment

Plastics have provided many societal benefits such as increased food production, improved hygiene, and preservation of materials and medications. However, there are concerns that many chemicals used in plastics can migrate into the environment, harming wildlife and humans (Box 1).<sup>1</sup>

Our understanding of the presence, abundance, and persistence of chemical additives in humans and the environment is still at an early stage. However, human biomonitoring studies in Europe have discovered a growing number of different hazardous chemicals present in human blood and body tissue. These include certain heavy metals, plasticisers, and flame retardants that originate from additives in plastic.<sup>2</sup> Understanding is also growing about how some population groups such as pregnant women and elderly people are particularly sensitive to chemicals with certain hazardous properties.<sup>3</sup>

### Box 1. Some consumer products with problematic additives

#### Clothes

Polyester, nylon and acrylic are forms of plastic and constitute more than 60% of the fabric on the clothing market. Consumers are mostly unaware of the use of toxic flame retardants in textiles, carpets, upholstery and furniture due to insufficient labelling requirements.<sup>6</sup>

#### Toys

Toys manufactured from thermo-mechanically recycled plastic from diverse sources can contain many banned, restricted or hazardous chemicals.<sup>6</sup> This is possible due to insufficient supply chain transparency, poor labelling, and inadequate regulation and monitoring of recycling operations.<sup>6</sup>

#### Plastic bottles

Some of the chemical additives often recovered from the environment include bisphenol A and nonylphenol (plasticisers used in the production of plastic bottles) and brominated flame retardants.<sup>7</sup>

The dispersion of chemicals additionally represents a hazard to the environment and wildlife.<sup>4</sup> It can be expected that plastics and their additives will be increasingly found in environmental matrices such as sediment, causing significant concern over time.<sup>5</sup>

### Tracing the consequences is complicated

Understanding the impact of additives and other chemicals from plastics on human health and the environment is complicated. Hundreds of thousands of raw materials and chemicals are used in plastics manufacturing, so mixtures of them may be present in everyday spaces like homes, schools and workplaces (Figure 1). Based on their global consumption, indicated by their total internationally traded tonnage, the most significant groups of additives,

in decreasing order, are: fillers, plasticisers, flame retardants, colorants, stabilisers, lubricants and surfactants (Box 2).<sup>8</sup> Given the nature of international supply chains, most of these substances are not controlled.

A further complication is the generation of non-intentionally added substances (NIAS), which can be impurities or degradation products of monomers, polymers and additives.<sup>9</sup> The hazards that these substances present on their own and in mixtures are unknown. To protect the environment and human health, there is a need to consider the risk-benefit ratio of chemical use, particularly when chemicals are just a component of a product, and not the product in themselves.<sup>1</sup>



**Figure 1. Chemical exposure from ordinary household objects**

An ordinary household is likely to have many plastic objects containing chemicals with known or suspected toxicity, including in clothes, toys, electronics and food containers.<sup>6</sup> Dibutyl phthalate (DBP) and bisphenol A (BPA) are used as plasticisers. In some countries BPA is banned, so bisphenol S (BPS) is used instead. Tris (2-chloroethyl) phosphate (TCEP) is used as flame retardant. Per- and polyfluoroalkyl substances (PFAS) are used as water repellents. Nonylphenol (NP) is used as a plasticiser.

## Box 2. Brief glossary of additives

### Fillers

Fillers reinforce plastics to improve their strength and heat resistance. Materials used as fillers include wood and glass fibres, but can be solid, liquid or gaseous substances that are added to a plastic.

### Plasticisers

Plasticisers improve the flexibility of plastics, whilst reducing hardness, viscosity and electrostatic charge.<sup>10</sup> Examples include phthalates, which are used in food packaging, cosmetics and flooring materials, and bisphenol A (BPA), found in the lining layer of aluminium cans.

### Flame retardants

Flame retardants are used to reduce flammability of consumer goods such as electronic devices and furniture. Brominated flame retardants (BFRs)<sup>11</sup> are amongst those that have caused the most concern<sup>1</sup> as well as being amongst the most common additives recovered from the environment.<sup>5</sup> High levels of flame retardants along with high levels of dioxins are typically detected in black plastic parts of personal electronic equipment and black plastic trays.<sup>6</sup>

### Colourants

Colourants enhance aesthetics and reduce light permeability. Different colourants include soluble dyes as well as organic and inorganic pigments.<sup>12</sup> Common organic pigments include cobalt(II) diacetate, whilst common inorganic pigments include cadmium, chromium and lead compounds.<sup>12</sup>

### Stabilisers

Stabilisers are used to prolong the useful life of plastics by protecting them against various sources of structural stress. Stabilisers have many functions: they can be antioxidants, heat stabilisers, UV stabilisers and biocides amongst others. This large variety demonstrates the complexity in categorising additives.

### Lubricants

Lubricants and slip agents prevent adhesion of plastic to processing equipment, improve fluidity and reduce surface friction. Groups of chemicals typically used as lubricants include waxes, metal soaps and fatty acid amides.<sup>12</sup>

### Surfactants

Surfactants find multiple uses such as wetting or antistatic agents and sometimes as dispersion agents in biocides or colourants, in which they and their degradation products can form a group of highly hazardous substances.<sup>8</sup> One important market application is to prevent static electrification of electrical insulators.<sup>12</sup>

## The three characteristics of concern

To simplify discussing the thousands of possible combinations of additives in plastics, we have broken down their effects on human health and the environment into three main characteristics of concern. These are:

- Carcinogenic, mutagenic and reprotoxic (CMR) substances,
- Persistent, bioaccumulative, and toxic (PBT) substances,
- Endocrine disrupting chemicals (EDC).

### Carcinogenic, mutagenic and reprotoxic substances

Approximately 900 chemicals are known to cause cancer (carcinogenic), be capable of causing genetic mutation (mutagenic) or be toxic for reproduction (reprotoxic). These are referred to as CMR chemicals (Box 3).<sup>13</sup> Many of them are hardly studied, are not adequately regulated in many parts of the world, and some are even authorised for use in food-packaging plastics in some jurisdictions.<sup>14</sup> CMR chemicals can be released during production and use of plastics, which poses risks to human health, the environment, and recycling systems.

### Box 3. Additive groups that can exhibit carcinogenic, mutagenic and reprotoxic properties

Different types and functions of chemicals in which CMR properties have been observed:<sup>12</sup>

- Organic and inorganic pigments;
- Waxes employed as lubricants such as paraffin, carnauba and montan;
- The metal soaps group of lubricants, such as lead stearate and zinc stearate;
- Slip agents of the fatty acid amides group, including erucamide and oleamide.

### Persistent, bioaccumulative, and toxic substances

Persistent, bioaccumulative, toxic substances (PBTs) and very persistent, very bioaccumulative (vPvBs) substances do not degrade easily in the environment and tend to accumulate in fatty tissues in living organisms, and therefore increase in concentration up the food chain (Box 4). They have been linked to adverse health effects in humans and animals. These substances have different patterns of bioaccumulation in fish and birds depending on food source. A main concern with vPvBs is that even if emissions stopped in the short term, their concentration in the environment and in biota might not necessarily decrease. In the long term, these cumulative effects lead to uncertainty of the predicted environmental concentration.<sup>15</sup>

Another large group of concern includes chemicals known as Persistent Organic Pollutants (POPs), regulated by the Stockholm Convention,<sup>16</sup> such as many brominated flame retardants. Some chemicals are banned but many are still to be addressed under the Convention, which requires ongoing updates.

### Box 4. Additive groups that can exhibit persistent, bioaccumulative, and toxic properties

#### Brominated flame retardants

They are persistent in the environment and can stay in the body for several years. A number now have restricted uses or are banned, which will allow environmental levels to decrease gradually.<sup>1</sup>

#### UV stabilisers

Phenolic benzotriazoles have been characterised as persistent, bioaccumulative, and toxic substances (PBTs) and as persistent organic pollutants (POPs).<sup>12</sup>

#### Plasticisers

Some chlorinated paraffins are classified as PBTs, but this depends on their carbon chain length.<sup>17</sup> Short chain chlorinated paraffins (10–13 carbon atoms in the chain) are widely classified as PBTs, and their use is restricted. Medium chain chlorinated paraffins (14–17 carbon atoms in the chain) have also been shown to be toxic to the environment. They are produced in higher quantities, but they are less widely studied and their use is not restricted.

#### Per- and polyfluoroalkyl substances

Long-chain PFASs have been found to be persistent, bioaccumulative and toxic;<sup>18</sup> however, not all of them have been classified or identified as substances of very high concern (SVHCs) in Europe for these properties.<sup>19</sup> Unlike typical POPs, perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) do not accumulate in fatty tissues but instead bind to proteins and thus accumulate mainly in organs such as the liver, kidney, brain and spleen.<sup>6</sup> In animal studies PFOS has been found to cause cancer, neonatal mortality, delays in physical development and endocrine disruption.<sup>20</sup>

## Endocrine disrupting chemicals

The substances that individually or in mixtures interfere with the way the hormonal system influences body processes are known as endocrine disrupting chemicals (EDCs) (Box 5). Their main impacts include:<sup>21</sup>

- ‘Hormone mimics’ eliciting a response in the body that a natural hormone would have induced.
- Blocking natural hormones from performing their function.
- Increasing or decreasing the levels of hormones in the bloodstream by affecting how they are made, broken down, or stored in the body.
- Changing how sensitive the body is to different hormones.

Because of their ability to disrupt many different hormones simultaneously, EDCs have been linked to numerous adverse human health outcomes, for example: alterations in sperm quality and fertility, abnormalities in sexual organ development, endometriosis, early puberty, altered nervous system function, altered immune function, certain types of cancer, respiratory problems, metabolic disruption, diabetes, obesity, cardiovascular problems, abnormal growth, and neurological and learning disabilities.<sup>21</sup>

### Box 5. Additive groups that can exhibit endocrine disrupting properties

#### Plasticisers

Plasticisers have been found to leach from finished products, which can lead to changes in their abundance in the human body, increasing the risk of long-term health concerns.<sup>22</sup> Several phthalates can disrupt the endocrine system even at low concentrations.<sup>4</sup> Bisphenol A (BPA) has been reported to have the potential to leach from food packaging.<sup>8</sup> In humans, BPA is linked to, amongst other things, reduced egg quality in female patients seeking fertility treatment.<sup>6</sup> Studies of human exposure to BPA and 4-tertiary-octylphenol in the United States found a correlation between concentration and specific demographic groups. For instance, females had statistically higher concentrations than males, children had higher concentrations than adolescents, adolescents had higher concentrations than adults, and the lowest concentrations were found in participants from the highest income groups.<sup>23</sup>

#### Antioxidants

The antioxidants butylated hydroxytoluene and butylated hydroxyanisole are used extensively in commodity plastics such as polyolefins, e.g. polyethylene.<sup>24</sup> They have been reported to affect the oestrogen hormone system *in vitro*.<sup>25</sup> The *in vivo* picture is less clear.<sup>26</sup>

#### Biocides

Biocides have been observed to have multiple effects. Two examples from the carbamate group, such as ziram and thiram, as well as triclosan, of the phenolic group, have been found to pose human and environmental health hazards and to show endocrine disrupting properties.<sup>8</sup>

#### Brominated flame retardants

BFRs are officially classified as endocrine disrupting chemicals (EDCs) and although they have a low acute toxicity, the human health concern is long-term interference with the thyroid hormone system because of their structural similarity to endogenous hormones. They also tend to accumulate in lipid and can be found in human breast milk at levels up to 400 times higher than in blood.<sup>1</sup> Exposure to BFRs is mostly through food but also from household dust. The highest dietary exposure in the European population tends to be from fish.<sup>1</sup>

#### UV stabilisers

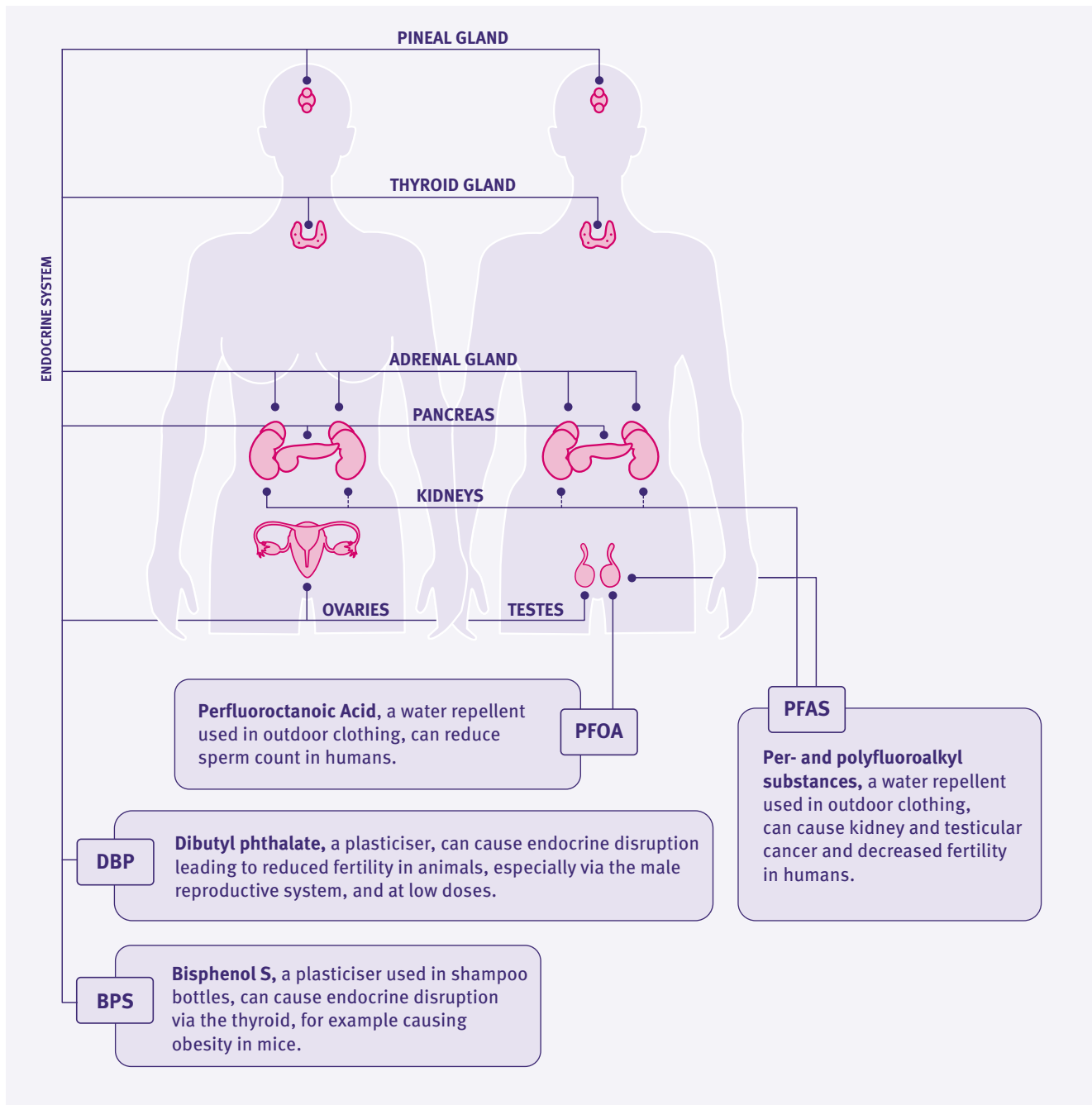
Notable examples of UV-stabilisers that have been identified as EDCs are benzophenones.<sup>12</sup>

#### Per- and polyfluoroalkyl substances

PFAS, polybrominated diphenyl ethers and organophosphate esters are associated with thyroid disease, infertility, and impaired development.<sup>27</sup>

#### Nonylphenol

Nonylphenol is used as antioxidant and plasticiser and has been found to leach from plastic bottles.<sup>28</sup> The production and use of nonylphenol and its ethoxylates are prohibited in Europe.<sup>29</sup>



**Figure 2.** Examples of endocrine disrupting chemicals<sup>6,12</sup> and the organs they affect.

Data sources: PFOA,<sup>30</sup> PFAS,<sup>31,32</sup> DBP<sup>33</sup> and BPS.<sup>34</sup>

## What we are currently doing wrong

### Wrong definitions and reactive approaches

Chemical additives have traditionally not been regulated to protect human and environmental health until damage has been proven, at which point a new unregulated substitute is introduced and the process is repeated.<sup>6</sup>

### *Insufficient data, transparency, and disclosure*

Good quality data on chemical inputs, toxicity and environmental impacts in different plastic applications are scarce and difficult to obtain, due to either the complexity of supply chains or to commercial confidentiality.<sup>8</sup>

This scarcity makes it difficult to characterise hazard levels and exposure profiles, particularly where many

plastic products are used simultaneously. The lack of data and transparency on plastic packaging is even more pronounced in parts of the value chain that include components such as adhesives, coatings, and inks, which exhibit severe data gaps on their constituent chemicals.<sup>8</sup> At the same time, to enable production of safer plastic objects and use of recycled material there is an urgent need to base risk assessments on actual data about composition of objects rather than estimates.<sup>8</sup>

#### *Incompletely harmonized toxicological information*

Difficulties in tracking toxicological information persist despite significant international efforts such as the European Classification, Labelling and Packaging (CLP) Regulation.<sup>35</sup> The CLP is based on the Globally Harmonised System of the United Nations<sup>36</sup> and it aims to ensure a high level of protection of health and the environment as well as safe trade of substances.<sup>37</sup> However, CLP hazard classifications are currently not available for many chemicals associated with plastic packaging, even for substances for which hazards have already been characterised.<sup>8</sup>

#### *Complex regulatory processes*

Building regulations that are fit for purpose is still a challenge. For example, in the EU alone there are approximately 40 legislative instruments including the Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH),<sup>38</sup> the CLP,<sup>35</sup> as well as legislation addressing the safety of toys, cosmetics, biocides, plant protection products, food and carcinogens in the workplace, amongst others.<sup>3</sup>

After Brexit on 1 January 2021, EU REACH registrations held by businesses in Great Britain (but not Northern Ireland) were carried across directly into UK REACH.<sup>39</sup> UK-based businesses were required to re-register their products with UK REACH during a transitional period. The deadlines for providing the required data packages have already been extended by three years. The Health and Safety Executive is also consulting on an alternative transitional registration model, to reduce the costs of supporting UK REACH registrations in addition to EU REACH registrations. The Department for Environment, Food and Rural Affairs (DEFRA) is coordinating a project to improve UK REACH, through a series of stakeholder workshops in 2022. This work is running alongside the development of the UK Chemicals Strategy, to be published in 2023.<sup>40</sup> UK REACH maintains EU REACH's aims and principles including the 'no data, no market' principle, the 'last resort' principle on animal testing, the principle of access to information for workers, and the precautionary principle.

A crucial policy gap is that polymers, the building blocks of plastics, are not subject to registration under REACH.<sup>3</sup> In fact, a comprehensive information base on all substances in the market is still lacking, which hinders the proper management of chemicals and products. For example, improving the efficiency of REACH evaluations whilst strengthening information requirements on critical hazards at all production levels needs to be part of the efforts to improve environmental and public health.<sup>3</sup>

## Wrong testing

#### *Isolated substance-by-substance risk assessment*

In substance-by-substance risk assessments, it is assumed that chemicals are released into a pristine environment or organism without any other chemicals present.<sup>41</sup> This is likely to miss many other intentionally or unintentionally added components and their interactions.<sup>12</sup> Unlike the pharmaceutical industry, which is expected to be aware of drug-drug interactions in patients, the chemical industry is not expected to be aware of interactions between chemicals.<sup>41</sup> In some cases, the safety of intentional chemical mixtures for particular uses (e.g. paint) has been assessed, but the consequences of unintentional coincidental exposure to multiple chemicals from different sources over time has not been assessed (Figure 3).<sup>3</sup> In this way, when separately evaluated substances coincide in an organism, e.g. in closed environments, the combined risk is drastically underestimated.<sup>41</sup>

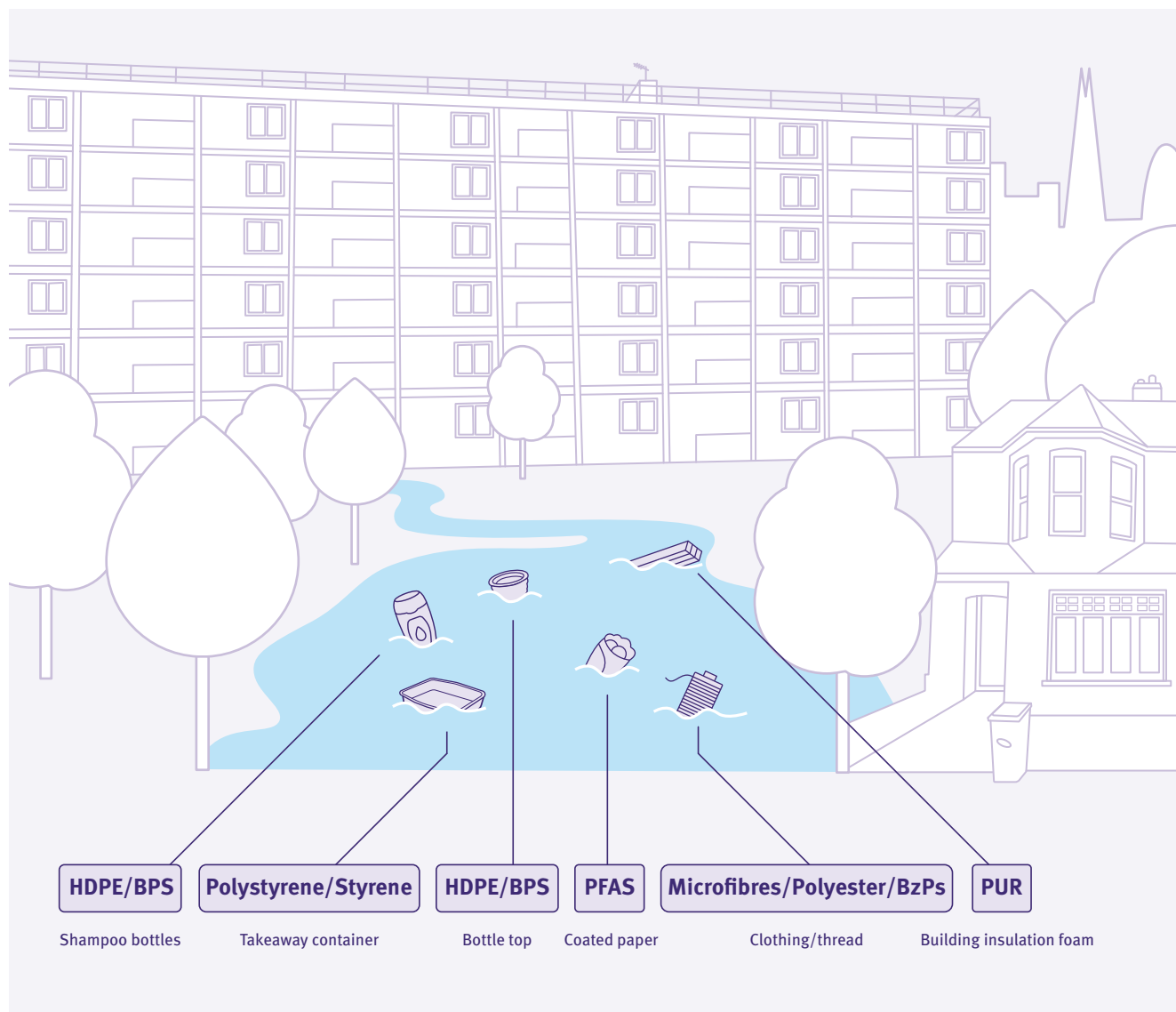
#### *Lack of exposure data and testing*

There is very little reliable data on the patterns of use of chemicals in the real world, so it is very difficult to carry out exposure-based risk assessments, as filling the data gaps using a scientific approach is practically impossible outside industry.<sup>8</sup> Although some industry-led projects have tried to address the gaps, the ability to supplement them with exposure data remains limited. Thus, the feasibility of moving beyond more basic hazard assessments for large numbers of chemicals is still unclear.<sup>8</sup>

#### *Assumed monotonicity of dose response relationships*

Most risk assessments assume that the higher the concentration and the exposure, the higher the risk of adverse health impacts. One consequence of using this toxicology paradigm is that the effects of untested chemicals likely to be taken up at low levels through the breath or through the skin are considered insignificant. However, the dose-response relationships of toxic substances are often non-monotonic, i.e., low doses can elicit adverse effects that are not observed at higher doses.<sup>43</sup> This risk assessment strategy therefore underestimates the real risk of exposure at low doses.





**Figure 3. Plastic additives in the environment**

An illustration of some of the most common plastic items identified in the river Thames in London,<sup>42</sup> with a selection of typical chemical additives and NIAS which may migrate into the environment, and subsequently be incorporated into the human food chain via fish. These include an HDPE bottle for shampoo (contains BPS), a polystyrene take-away container (containing the monomer styrene as a NIAS), a bottle top made of high density polyethylene (HDPE, also contains BPS), take-away food boxes and wrappings in coated paper (contains PFAS), polyester microfibres (containing benzophenones (BzPs) as UV stabilisers), and fragments of building insulation foam made of polyurethane (PUR) and containing the latest flame retardants.

## Box 6. Key examples of regrettable substitutions associated with plastic packaging

### Bisphenols<sup>8</sup>

Bisphenol A (BPA) is widely used in some polycarbonate plastics and epoxy coatings and has been classified as an EDC under REACH, in addition to several pre-existing harmonised CLP classifications as a human health hazard.<sup>8</sup> Chemicals such as bisphenol S (BPS) and bisphenol F (BPF) have been used as alternatives, although their endocrine activities are, predictably, very similar to those of BPA.<sup>45</sup> The safety of these substitutions is highly questionable and may represent a health threat.<sup>46</sup> The UN Environment Programme<sup>47</sup> recognised BPS and BPF as EDCs or potential EDCs but the equivalent classifications under REACH seem to be lagging.<sup>8</sup> A similar situation applies to the ortho-phthalate group, as some phthalates are classified as EDCs within REACH, while others, some of which were recognised by UNEP, are not.

### Per- and polyfluoroalkyl substances<sup>18</sup>

GenX, a perfluoroether, has been available as a PFAS substitute since 2012, however, there are concerns about its persistence, accumulation potential and toxicity.<sup>48</sup> Under environmentally relevant conditions, perfluoroether chains were found to be as resistant to abiotic and biotic degradation as perfluoroalkyl chains, suggesting that GenX is as persistent as perfluorooctanoic acid (PFOA).<sup>49</sup> Surface-water influenced groundwater intake points within 25 km from a fluoropolymer manufacturing plant showed similar levels of GenX and PFOA in all samples.<sup>48</sup>

### Brominated flame retardants

BFRs are being replaced with retardants containing chlorines, which are bio-accumulative, persistent and likely to be found in the environment throughout the 21st century.<sup>1</sup>

## Substituting one harmful chemical with another

The main cause for regrettable substitutions<sup>44</sup> is where the banned substance and its replacement have similar structure and therefore comparable endocrine disrupting properties (Box 6 and Figure 4).<sup>8</sup>

## How can we make additives safer?

### The need for action and coordination

The case for action on chemical additives is clear, because under current manufacturing and recycling regulations, undesirable combinations of chemicals still occur in personal use products. This is due to a lack of concerted action.<sup>8</sup> It is no longer viable to work with non-harmonised classifications. New processes are needed to streamline the registration under UK REACH of chemicals that have a recommended classification under another internationally reputable register.

## Build on international regulation

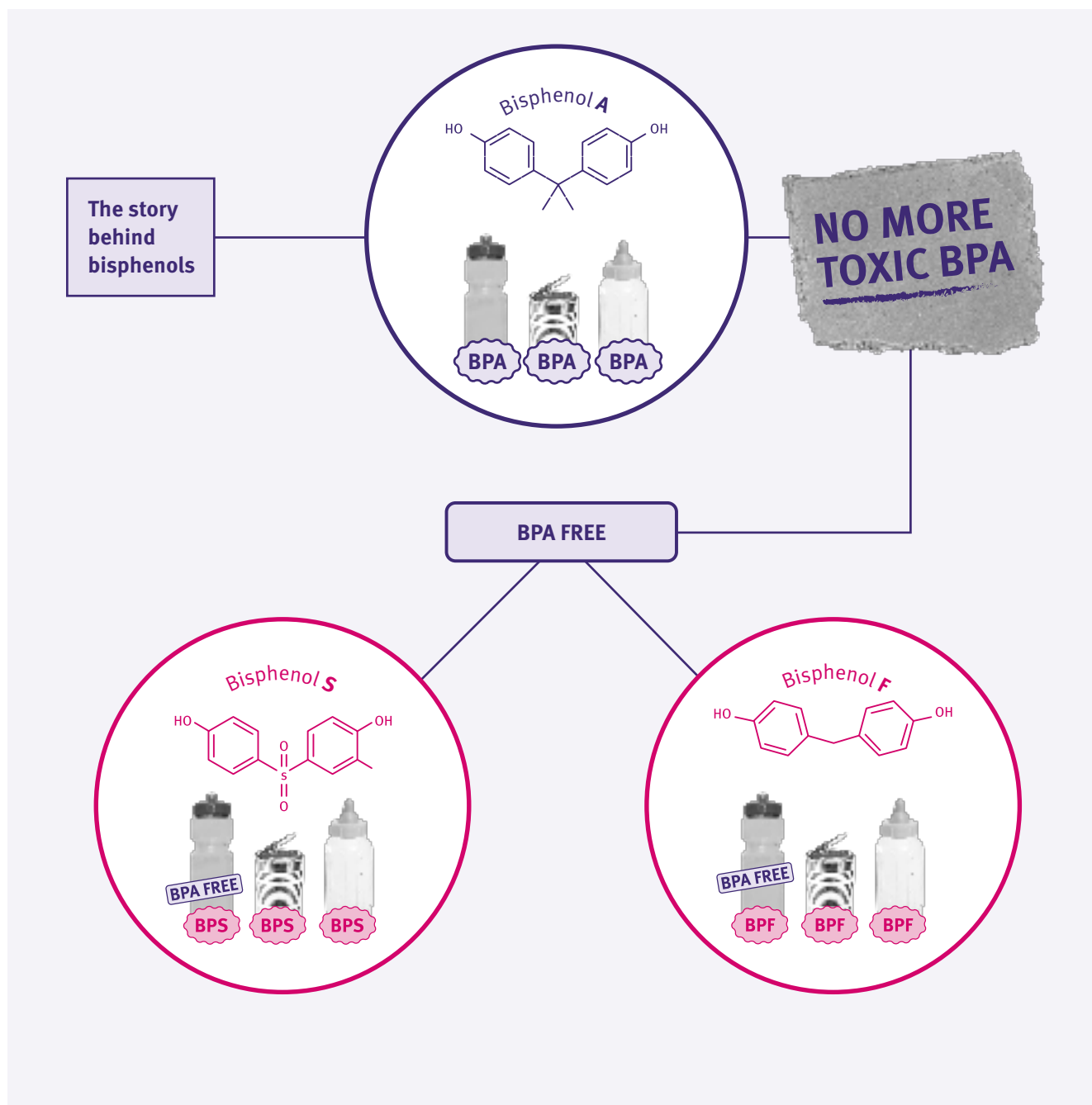
Internationally recognised sources that classify chemicals as EDC, PBT (or vPvB) and CMR substances that have been or are used as additives include:

- the CLP<sup>35</sup> by the European Chemicals Agency;
- the Danish voluntary CLP classifications<sup>50</sup> by the Danish Environmental Protection Agency based on *in silico* models;
- International Panel on Chemical Pollution of the United Nations Environment Programme.<sup>47</sup>

## Build on three relevant international conventions

There are three global chemicals and waste conventions that aim to help in identifying, substituting and managing toxic additives. They are also relevant for international efforts to address marine plastic litter, pollution by microplastics and the management of plastic wastes. The conventions are:<sup>6</sup>

- the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal,<sup>51</sup>
- the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade,<sup>52</sup>
- the Stockholm Convention on Persistent Organic Pollutants.<sup>16</sup>



**Figure 4.** A key regrettable substitution: bisphenols (Box 6)

BPA and its replacements BPS and BPF have very similar chemical structures, and similar metabolism, potency and mechanisms of action, though much less data is available on the behaviour of BPS and BPF compared to BPA.<sup>45</sup> Regulation of additives by structural group would avoid replacing a chemical classified as a human health hazard with others likely to have similar health impacts but for which this data is not yet available.

## What does policy need to do?

### Improve risk assessments

To enable better use of plastic, we need to better understand the toxicity of what it contains and how it can affect human and environmental health. To identify and certify what is safe, the causes, mechanisms and pathways of toxicity that start with the use of additives must be understood. This requires transparency about what individual products contain, improving assessments of the toxicity of mixtures, and considering non-monotonic dose responses.

#### *Improve transparency*

Avoiding the use of toxic chemicals requires the availability of information on the composition of plastic objects, which is a challenge due to the complexity of global supply chains. Product manufacturers, consumers and recyclers have the right to make informed decisions and provide market demand for safe alternatives. Despite the urgency for this transparency, when unable to demonstrate a commercial interest, the research community has previously encountered difficulties in accessing industrial information.<sup>8</sup> In future, disclosure and labelling schemes of plastic objects should include more information on the additives they contain.<sup>6</sup>

#### *Improve assessments of mixture toxicity*

New techniques to analyse mixtures help to evaluate the effects of unknown NIAS and account for mixture toxicity. Thus, the overall quantity of substances migrating from a given packaging object can be tested for multiple types of toxicity using, e.g. *in vitro* systems.<sup>53</sup> Improving understanding of mixture toxicity also requires more widespread assessments of mixtures in recycled materials, particularly those in food contact applications.<sup>54</sup> In fact, because of international recognition of mixture toxicity there are now attempts to include it in legislation fields such as food additives, toys, food contact material, detergents and cosmetics.<sup>3</sup>

#### *Address non-monotonic dose responses*

It is worth highlighting two recent changes in approach to address non-monotonic dose-response relationships. First, the U.S. National Research Council<sup>55</sup> proposes to use, as far as feasible, evidence tables and graphics with consistent units and scales providing more context for exposure ranges. Second, the Danish Centre on Endocrine Disruptors advocates using a non-threshold approach as the default in assessing the toxicity risk of EDCs, unless strong evidence for a threshold is available.<sup>50</sup>

### Improve the toxicity knowledge base

#### *Expand mapping by the European Chemicals Agency*

The European Chemicals Agency's (ECHA) mapping of additives already includes substances registered under REACH of which more than 100 tonnes per year are produced or imported.<sup>56</sup> This helps companies prioritise instances where safe-use information along the supply chain should be improved.<sup>56</sup> Innovation and safe substitution can be improved internationally by replicating the goals of the ECHA mapping such as: monitoring the improvement in quality of registrations of safe additives, and implementing guidance for businesses on how to characterise the uses of additives in plastics.

#### *Enhance biomonitoring*

The analysis of blood, urine and hair samples of volunteers, i.e. biomonitoring, is a recognised tool in identifying what chemicals people are actually exposed to. This helps to estimate risks from coincidental chemical mixtures by monitoring the levels of toxic compounds in volunteers' bodies over time.<sup>41</sup> Biomonitoring is crucial to better understand of exposure levels on a population scale, which hinges on the ability to monitor large numbers of volunteers (Box 7). Therefore, it is important to support UK and international human and environmental biomonitoring capacities, complementing ecosystem monitoring initiatives similar to what is foreseen in the European Chemicals Strategy.<sup>3</sup>

### Box 7. Progress in biomonitoring

In 2019, biomonitoring helped inform the reduction of acceptable exposure thresholds of four phthalate compounds (butyl benzyl phthalate, di(2-ethylhexyl) phthalate, dibutyl phthalate and diisobutyl phthalate), which are found in products such as floorings, mattresses and footwear, and are known to impair male sexual development and fertility.<sup>41</sup> Examples of biomonitoring good practice include the US programme started in the 1960s, the programme in Germany started in the 1980s, and more recently the European Human Biomonitoring Initiative or HBM4EU.<sup>41,57</sup>

### *Regulate by group*

Myriad administrative and public health costs arise when a chemical is phased out after years of research and negotiation, only to be replaced by others which turn out to exhibit similar toxic properties. Managing substances by structural group can be more efficient because of the large number of chemicals in use and the effort that fully characterising their individual environmental and human health impacts would entail.

Acknowledging that it is not practicable to assess an overwhelming number of possible mixtures and that their effects need to be integrated into risk assessments, a generic approach to risk management (GARM) can be beneficial.<sup>3</sup> An example of this is the European Roadmap (Box 8). GARM offers a simpler preventive approach that sends clear signals to enforcement authorities, industry and downstream users on the types of substances where

#### **Box 8. European Roadmap to assess and restrict harmful chemicals by group**

The European Commission has stated that it will prioritise harmful substances for restrictions for all uses through grouping, instead of one by one, which helps address the associated challenges of mixture toxicity and regrettable substitutions.<sup>3</sup> The 'restrictions roadmap' outlines the phase-out of a broad range of harmful chemicals by 2030. It includes a 'rolling list' of restrictions that have been planned for the most harmful substance groups that meet the criteria for CMRs, PBTs, vPvBs, EDCs and immunotoxicants. One of the aims is to allow industry and other stakeholders to be better prepared for potential upcoming restrictions.

This approach has the potential to improve the safety of most manufactured products and lower the chemical intensity of closed spaces such as schools, homes and workplaces. The roadmap arises in a context where international regulatory agencies are increasingly applying grouping approaches to hazard and risk assessments for, e.g. pesticides and food flavourings, and are planning to apply them to more chemicals in the future.<sup>8</sup> The broader scope within the roadmap could lead to 7,000 chemicals being banned by 2030 and should help phase out the practice of tweaking chemical formulations slightly to circumvent restrictions.<sup>58</sup>

innovation should be prioritised. In the European context, GARM automatically triggers pre-determined measures including restrictions and bans based on hazardous properties of a chemical and generic considerations of its exposure such as use in products for children. Increasing evidence combined with public concern indicate that GARM should become the default option for the most harmful chemicals, particularly in consumer products.

To manage chemicals by group, the Health and Safety Executive of the UK should also exploit substance registration data to enable grouping by chemical structure. This function is essential to facilitate substitution of chemicals of concern and help prevent regrettable substitutions.<sup>59</sup>

The HSE could disseminate information on substance groups identified under a suitable screening process to help downstream users who are considering substituting hazardous substances, materials or products.

### **Promote non-toxic chemicals in production systems**

For cleaner production and recycling of plastics to become realistic, policies are needed to improve the quality of the first-time production of goods, as all materials containing toxic substances in a recycling stream undermine the quality and safety of the recycle.<sup>54</sup> Therefore, separate targets are required for production/recovery streams without toxic components, in addition to streams that are likely to be contaminated with toxic chemicals.

### *Extended producer responsibility*

In a growing number of countries, it is unacceptable to argue that producers have no responsibility for the safety and recoverability of products. Several governments recognise the benefit of placing responsibility for post-consumer goods on producers.<sup>60</sup> Producers can manage the hazardous materials they put on the market using extended producer responsibility (EPR) schemes, that require them to establish collection systems for their own waste to fulfil take-back mandates and achieve recycling targets. Usually, a fee-charging producer responsibility organisation (PRO) operates the scheme nationally on behalf of producers. Better use of EPR can prevent unintended shifts to unrecyclable materials when combined with landfill tax and tipping fees, incineration gate fees, taxes on unrecycled material, on virgin plastic resin, on single-use plastics, and subsidy reductions for oil and gas.<sup>61</sup> However, a condition for best results is to measure success not only by quantity but also by the quality of recovered material.

## Support for innovation in materials and technology

There is a pressing need for UK and international governments to develop safer materials that displace those with hazardous additives or recycled plastic with unidentified toxic mixtures. Additional non-toxic alternatives should be developed as in the example of the ongoing work on alternatives for short-chain chlorinated paraffins and decabromodiphenyl ether within the Stockholm Convention.<sup>6</sup>

## Finding chemical and functional alternatives

'Functional substitution' removes the focus on properties and focuses on the technical functions of the substance, making substitution an innovative activity that

creates commercial and environmental benefits. Introducing non-hazardous substances whilst preserving functionality requires procedural or organisational changes. Whenever no viable safer alternatives are known, connecting value chain stakeholders with scientists can help transition to safer chemicals, for example through supply chain workshops involving international authorities, industry associations, and NGOs working on substitution. It is worth remembering that although they have less technical knowledge on substances, downstream users can specify and demand safer alternatives from their suppliers. Some examples are listed in Box 9.

### Box 9. Examples of mechanisms for promoting functional substitution of chemicals

#### The "Substitute it now!" list

Substituting chemicals safely entails identifying hazardous chemicals as well as structurally similar chemicals with likely similar toxicity. The regularly updated SIN (Substitute It Now!) List indicates chemicals that should be phased out immediately. These are hazardous chemicals, used in a wide variety of objects and products, which have been evaluated by the International Chemical Secretariat, ChemSec, as meeting criteria for SVHCs under the REACH definitions.<sup>62</sup>

#### TCO Certified

Hazardous substances in phones, computers and other information and communications technology products are a risk to human health. The TCO certification standard was created to guarantee that ICT products purchased by employers met environmental standards and were sufficiently ergonomic. TCO Certified works on the principle that simply banning substances is not enough and better information about substitutes is required, assuming that a chemical is considered a high risk until it is proven

not to be. TCO provides a list of accepted substances and guidance to achieve certification.<sup>63</sup>

#### The Marketplace platform

Marketplace is a platform where suppliers and buyers can offer and find safer alternatives to hazardous chemicals as an important first step in the substitution process. It can help businesses ensure future REACH compliance by facilitating advertisements of safer alternatives.<sup>64</sup>

#### OECD QSAR Toolbox

The OECD QSAR Toolbox is software designed to fill gaps in human and environmental toxicity data needed for assessing the hazards of chemicals. It includes a logical workflow that groups chemicals into categories to allow users to develop new products and chemicals whilst avoiding regrettable substitution.<sup>59</sup> The main functions of the Toolbox are:<sup>65</sup>

- To identify relevant structural characteristics or mode of action of a target chemical,
- To identify chemicals that have the same structural characteristics and/or mode of action,
- To use existing experimental data to fill the data gaps.

## Options for action by stakeholders

### System realignment

Industrial stakeholders with a conventional business model and public health responsibilities that stop at the factory gate often regard waste management, and more recently recycling, as the solution to plastic pollution. Although end-of-life interventions help to contain some waste leakage internationally, they do not help to reduce the surplus of plastic beyond the essential and do not reduce the release and intake of toxic additives. Unless the framing of responsibility for industrial stakeholders changes, the incentive for systems to realign will remain limited.

### Standards

Guidance through standards created in collaboration between industry, government, international organisations and civil society has already led to effective substitutions. For instance, building renovations using safer materials have reduced concentrations of PFAS, polybrominated diphenyl ethers, and organophosphate esters in dust from offices compared to spaces without interventions.<sup>27</sup> It is essential to ensure that international scientific data becomes easily accessible for safety assessments and to inform regulation. Several options within the Basel, Rotterdam and Stockholm Conventions are ideal to promote the sound management and safe removal of chemicals, and can create enough demand to make safer materials competitive.

### New business models to reduce plastic waste

There remains a great need for work on development and implementation of techniques to mainstream new commercial models. All of them can support the material value preservation required for improved human and environmental health. Examples include:

- Product-service systems, whereby embedded material is not traded but only the functionality, incentivising high-quality durable materials in many reuse modalities,
- Remanufacturing through company take-back programmes,
- Right-to-repair regulations, where options for repair of customer-owned items are available,
- Discouraging built-in obsolescence through positive incentives or penalising measures.

### Disclosure of materials and chemicals

Commercial confidentiality and the difficulty in tracking materials several stages upstream are the two main hurdles to achieving disclosure and transparency about additive content in any given plastic-containing product. At the same time, knowing the critical properties of substances is essential for chemical companies to understand the long-term viability of their portfolio, as investors start to include sustainable chemistry in their risk assessment. In addition, this knowledge will help companies integrate substitution in future operations. In the long run, increased chemical disclosure can help UK and international businesses remain competitive and at the forefront of technological developments. To address confidentiality, a demand-led approach is needed, where customers expect more information, and brand owners gradually disclose and require compliance from their suppliers until value chains are significantly covered (Box 10).

#### Box 10. Apple's Full Material Disclosure programme

Apple started the Full Material Disclosure programme in 2015, where it shares the chemical composition of components used in its electronics.<sup>66</sup> Such initiatives demonstrate that additional companies in other sectors can follow Apple's example. The company has gradually replaced phthalates that were used in power cords and headphone cables before 2013 with alternatives such as thermoplastic elastomers. It claims its current products are free of PVC and phthalates, except those manufactured in South Korea and India where it is seeking government approval for replacements.<sup>67</sup>

## Conclusion

The leakage of plastic additives into the environment and subsequent uptake by organisms is a serious problem, and yet plastics are an essential component of 21st century lives across the world. To enable better use and reuse of plastic, we need to better understand the toxicity of what it contains and how it can affect human and environmental health. UK and international human and environmental biomonitoring initiatives are an important step towards this.

Delivering new, safe alternatives to existing additives requires improved material design, advances in toxicology, new business models, and the better use of international conventions and similar policy instruments. Ideally, these should create a transparent market for substances, materials and products for a better environment.

Analysis and management of substances by group, as proposed in the EU, will be a cornerstone in the effort to prevent regrettable substitutions and to lighten the burden of managing the toxicity of chemical mixtures.

### The need for a transdisciplinary approach

The molecular science and engineering approach is central to reducing harm from toxic additives in plastics. It is needed to:

- develop new molecules to deliver properties such as UV-light resistance, flame retarding properties, and colour, but without the toxic hazards of existing additives,
- develop and improve methods to monitor the presence of additive molecules and their derivatives in the environment and in organisms. These technologies should be capable of identifying very low threshold concentrations and be non- or minimally invasive.
- develop and improve methods to measure or model the interaction of potential toxicants in real world situations,
- develop new processes to reduce leakage of additives into the environment, for example by improving plastic manufacturing and recycling.

## Acronyms

<b>BPA</b>	Bisphenol A
<b>BPF</b>	Bisphenol F
<b>BPS</b>	Bisphenol S
<b>BFRs</b>	Brominated flame retardants
<b>CMR</b>	Carcinogenic, mutagenic and reprotoxic
<b>CLP</b>	Classification, Labelling and Packaging Regulation
<b>EDC</b>	Endocrine disrupting chemicals
<b>EPR</b>	Extended producer responsibility
<b>GARM</b>	Generic approach to risk management
<b>NIAS</b>	Non-intentionally added substances
<b>PFAS</b>	Per- and polyfluoroalkyl substances
<b>PFOS</b>	Perfluorooctane sulfonate
<b>PFOA</b>	Perfluorooctanoic acid
<b>POPs</b>	Persistent Organic Pollutant
<b>PBT</b>	Persistent, bioaccumulative, and toxic
<b>PRO</b>	Producer responsibility organisation
<b>REACH</b>	Registration, Evaluation, Authorisation and Restriction of Chemicals Regulation
<b>SVHCs</b>	Substances of very high concern
<b>vPvB</b>	Very persistent, very bioaccumulative



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## References

- Gant TW, Smith HE, Marczylo EL, *et al.* (2018) 21<sup>st</sup> century chemicals. In Dalton ARH (Ed.), *Annual report of the Chief Medical Officer 2017. Health impacts of all pollution – what do we know?* (pp. 46–63). London: HM Government. [assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/690846/CMO\\_Annual\\_Report\\_2017\\_Health\\_Impacts\\_of\\_All\\_Pollution\\_what\\_do\\_we\\_know.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/690846/CMO_Annual_Report_2017_Health_Impacts_of_All_Pollution_what_do_we_know.pdf). Accessed: 16 September 2022.
- Directorate-General for Environment (European Commission), Milieu Ltd, Risk & Policy Analysts (RPA), *et al.* (2017) *Study for the strategy for a non-toxic environment of the 7th Environment Action Programme: final report*. Brussels: European Commission. [op.europa.eu/en/publication-detail/-/publication/89fbbb74-969c-11e7-b92d-01aa75ed71a1/language-en](https://op.europa.eu/en/publication-detail/-/publication/89fbbb74-969c-11e7-b92d-01aa75ed71a1/language-en). Accessed: 16 September 2022.
- European Commission, Directorate-General for Environment (2020) *Chemicals strategy for sustainability: Towards a toxic-free environment*. COM(2020) 667. Brussels: European Commission. [eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM%3A2020%3A667%3AFIN](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM%3A2020%3A667%3AFIN). Accessed: 1 August 2023.
- Oehlmann J, Schulte-Oehlmann U, Kloas W, *et al.* (2009) A critical analysis of the biological impacts of plasticizers on wildlife. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 364(1526), 2047–2062. [doi.org/10.1098/rstb.2008.0242](https://doi.org/10.1098/rstb.2008.0242).
- Hermabessiere L, Dehaut A, Paul-Pont I, *et al.* (2017) Occurrence and effects of plastic additives on marine environments and organisms: a review. *Chemosphere*, 182, 781–793. [doi.org/10.1016/j.chemosphere.2017.05.096](https://doi.org/10.1016/j.chemosphere.2017.05.096).
- Regional Activity Centre for Sustainable Consumption and Production (SCP/RAC) (2020) *Plastic's toxic additives and the circular economy*. [ipen.org/documents/plastics-toxic-additives-and-circular-economy](https://ipen.org/documents/plastics-toxic-additives-and-circular-economy). Accessed: 1 August 2023.
- Bergé A, Cladière M, Gasperi J, *et al.* (2012) Meta-analysis of environmental contamination by alkylphenols. *Environmental Science and Pollution Research*, 19(9), 3798–3819. [doi.org/10.1007/s11356-012-1094-7](https://doi.org/10.1007/s11356-012-1094-7).
- Groh KJ, Backhaus T, Carney-Almroth B, *et al.* (2019) Overview of known plastic packaging-associated chemicals and their hazards. *Science of the Total Environment*, 651, 3253–3268. [doi.org/10.1016/j.scitotenv.2018.10.015](https://doi.org/10.1016/j.scitotenv.2018.10.015).
- Nerin C, Alfaro P, Aznar M, *et al.* (2013) The challenge of identifying non-intentionally added substances from food packaging materials: A review. *Analytica Chimica Acta*, 775, 14–24. [doi.org/10.1016/j.aca.2013.02.028](https://doi.org/10.1016/j.aca.2013.02.028).
- Rosen SL (1993) *Fundamental principles of polymeric materials*. Hoboken: John Wiley & Sons.
- Talsness CE, Andrade AJ, Kuriyama SN, *et al.* (2009) Components of plastic: experimental studies in animals and relevance for human health. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 364(1526), 2079–2096. [doi.org/10.1098/rstb.2008.0281](https://doi.org/10.1098/rstb.2008.0281).
- Bridson JH, Gaugler EC, Smith DA, *et al.* (2021) Leaching and extraction of additives from plastic pollution to inform environmental risk: a multidisciplinary review of analytical approaches. *Journal of Hazardous Materials*, 414, 125571. [doi.org/10.1016/j.jhazmat.2021.125571](https://doi.org/10.1016/j.jhazmat.2021.125571).
- Muncke J (2021) Tackling the toxics in plastics packaging. *PLoS Biology*, 19(3), e3000961. [doi.org/10.1371/journal.pbio.3000961](https://doi.org/10.1371/journal.pbio.3000961).
- Wiesinger H, Wang Z, and Hellweg S (2021) Deep dive into plastic monomers, additives, and processing aids. *Environmental Science & Technology*, 55(13), 9339–9351. [doi.org/10.1021/acs.est.1c00976](https://doi.org/10.1021/acs.est.1c00976).
- European Medicines Agency (2015) *Guideline on the assessment of persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substances in veterinary medicinal products*. London: European Medicines Agency. [www.ema.europa.eu/en/assessment-persistent-bioaccumulative-toxic-pbt-very-persistent-very-bioaccumulative-vpvb-substances](https://www.ema.europa.eu/en/assessment-persistent-bioaccumulative-toxic-pbt-very-persistent-very-bioaccumulative-vpvb-substances). Accessed: 21 September 2022.
- Stockholm Convention on Persistent Organic Pollutants (POPs) (2019). [www.pops.int/TheConvention/Overview/TextoftheConvention/tabid/2232/Default.as](https://www.pops.int/TheConvention/Overview/TextoftheConvention/tabid/2232/Default.as). Accessed: 21 September 2022.

17. Glüge J, Schinkel L, Hungerbühler K, *et al.* (2018) Environmental risks of medium-chain chlorinated paraffins (MCCPs): a review. *Environmental Science & Technology*, 52(12), 6743–6760. doi.org/10.1021/acs.est.7b06459.
18. Scheringer M, Trier X, Cousins IT, *et al.* (2014) Helsingør statement on poly- and perfluorinated alkyl substances (PFASs). *Chemosphere*, 114, 337–339. doi.org/10.1016/j.chemosphere.2014.05.044.
19. Brendel S, Fetter É, Staude C, *et al.* (2018) Short-chain perfluoroalkyl acids: environmental concerns and a regulatory strategy under REACH. *Environmental Sciences Europe*, 30(1), 1–11. doi.org/10.1186/s12302-018-0134-4.
20. Fei C, McLaughlin JK, Lipworth L, *et al.* (2009) Maternal levels of perfluorinated chemicals and subfecundity. *Human Reproduction*, 24(5), 1200–1205. doi.org/10.1093/humrep/den490.
21. Ruiz D, and Patisaul H (2022) *Endocrine-disrupting chemicals (EDCs)*. www.endocrine.org/patient-engagement/endocrine-library/edcs. Accessed: 21 September 2022.
22. Gustafsson E, Bowden TM, and Rennie AR (2020) Interactions of amphiphiles with plasticisers used in polymers: Understanding the basis of health and environmental challenges. *Advances in Colloid and Interface Science*, 277, 102109. doi.org/10.1016/j.cis.2020.102109.
23. Calafat AM, Ye X, Wong L-Y, *et al.* (2008) Exposure of the US population to bisphenol A and 4-tertiary-octylphenol: 2003–2004. *Environmental Health Perspectives*, 116(1), 39–44. doi.org/10.1289/ehp.10753.
24. Tolinski M (2015) *Additives for polyolefins: getting the most out of polypropylene, polyethylene and TPO*. Waltham: William Andrew.
25. Pop A, Drugan T, Gutleb AC, *et al.* (2018) Estrogenic and anti-estrogenic activity of butylparaben, butylated hydroxyanisole, butylated hydroxytoluene and propyl gallate and their binary mixtures on two estrogen responsive cell lines (T47DKbluc, MCF7). *Journal of Applied Toxicology*, 38(7), 944–957. doi.org/10.1002/jat.3601.
26. Pop A, Kiss B, and Loghin F (2013) Endocrine disrupting effects of butylated hydroxyanisole (BHA-E320). *Clujul Medical*, 86(1), 16.
27. Young AS, Hauser R, James-Todd TM, *et al.* (2021) Impact of “healthier” materials interventions on dust concentrations of per- and polyfluoroalkyl substances, polybrominated diphenyl ethers, and organophosphate esters. *Environment International*, 150, 106151. doi.org/10.1016/j.envint.2020.106151.
28. Loyo-Rosales JE, Rosales-Rivera GC, Lynch AM, *et al.* (2004) Migration of nonylphenol from plastic containers to water and a milk surrogate. *Journal of Agricultural and Food Chemistry*, 52(7), 2016–2020. doi.org/10.1021/jf0345696.
29. Rani M, Shim WJ, Han GM, *et al.* (2015) Qualitative analysis of additives in plastic marine debris and its new products. *Archives of Environmental Contamination and Toxicology*, 69(3), 352–366. doi.org/10.1007/s00244-015-0224-x.
30. Joensen UN, Bossi R, Leffers H, *et al.* (2009) Do perfluoroalkyl compounds impair human semen quality? *Environmental Health Perspectives*, 117(6), 923–927. doi.org/10.1289/ehp.0800517.
31. Steenland K, and Winquist A (2021) PFAS and cancer, a scoping review of the epidemiologic evidence. *Environmental Research*, 194, 110690. doi.org/10.1016/j.envres.2020.110690.
32. Bach CC, Vested A, Jørgensen KT, *et al.* (2016) Perfluoroalkyl and polyfluoroalkyl substances and measures of human fertility: a systematic review. *Critical Reviews in Toxicology*, 46(9), 735–755. doi.org/10.1080/10408444.2016.1182117.
33. Czubacka E, Czerczak S, and Kupczewska-Dobecka M (2021) The overview of current evidence on the reproductive toxicity of dibutyl phthalate. *International Journal of Occupational Medicine and Environmental Health*, 34(1), 15–37. doi.org/10.13075/ijom.1896.01658.
34. Del Moral LI, Le Corre L, Poirier H, *et al.* (2016) Obesogen effects after perinatal exposure of 4, 4-sulfonyldiphenol (Bisphenol S) in C57BL/6 mice. *Toxicology*, 357, 11–20. doi.org/10.1016/j.tox.2016.05.023.

35. Regulation (EC) No 1272/2008 – classification, labelling and packaging of substances and mixtures (CLP). Official Journal L 353, 1 (2008). [eur-lex.europa.eu/eli/reg/2008/1272/2023-04-20](http://eur-lex.europa.eu/eli/reg/2008/1272/2023-04-20). Accessed: 21 September 2022.
36. United Nations Economic Commission for Europe (2021) *Globally harmonized system of classification and labelling of chemicals (GHS Rev. 9, 2021)*. [unece.org/transport/standards/transport/dangerous-goods/ghs-rev9-2021](http://unece.org/transport/standards/transport/dangerous-goods/ghs-rev9-2021). Accessed: 21 September 2022.
37. European Chemicals Agency (2022) *Understanding CLP*. [echa.europa.eu/regulations/clp/understanding-clp](http://echa.europa.eu/regulations/clp/understanding-clp). Accessed: 21 September 2022.
38. Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. Official Journal L396, 1–849 (2006). [data.europa.eu/eli/reg/2006/1907/oj](http://data.europa.eu/eli/reg/2006/1907/oj). Accessed: 1 August 2023.
39. Health and Safety Executive (n.d.) UK registration, evaluation, authorisation and restriction of chemicals (REACH). [www.hse.gov.uk/reach/index.htm](http://www.hse.gov.uk/reach/index.htm). Accessed: 10 February 2023.
40. Department for Environment, Food and Rural Affairs (2023) *Environmental Improvement Plan 2023: First revision of the 25 Year Environment Plan*. London: DEFRA. [www.gov.uk/government/publications/environmental-improvement-plan](http://www.gov.uk/government/publications/environmental-improvement-plan). Accessed: 28 June 2023.
41. Notman N (2021) A mixed problem. *Chemistry World*. [www.chemistryworld.com/features/how-should-chemical-mixtures-be-regulated/4013604.article](http://www.chemistryworld.com/features/how-should-chemical-mixtures-be-regulated/4013604.article). Accessed: 21 September 2022.
42. Bernardini G, McConville A, and Castillo AC (2020) Macro-plastic pollution in the tidal Thames: An analysis of composition and trends for the optimization of data collection. *Marine Policy*, 119, 104064. [doi.org/10.1016/j.marpol.2020.104064](https://doi.org/10.1016/j.marpol.2020.104064).
43. Vandenberg LN, Colborn T, Hayes TB, *et al.* (2012) Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. *Endocrine Reviews*, 33(3), 378–455. [doi.org/10.1210/er.2011-1050](https://doi.org/10.1210/er.2011-1050).
44. Maertens A, Golden E, and Hartung T (2021) Avoiding regrettable substitutions: Green toxicology for sustainable chemistry. *ACS Sustainable Chemistry & Engineering*, 9(23), 7749–7758. [doi.org/10.1021/acssuschemeng.0c09435](https://doi.org/10.1021/acssuschemeng.0c09435).
45. Rochester JR, and Bolden AL (2015) Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. *Environmental Health Perspectives*, 123(7), 643–650. [doi.org/10.1289/ehp.1408989](https://doi.org/10.1289/ehp.1408989).
46. Chen Y, Shu L, Qiu Z, *et al.* (2016) Exposure to the BPA-substitute bisphenol S causes unique alterations of germline function. *PLoS Genetics*, 12(7), e1006223. [doi.org/10.1371/journal.pgen.1006223](https://doi.org/10.1371/journal.pgen.1006223).
47. International Panel on Chemical Pollution (IPCP) (2017) *Overview Report I: Worldwide initiatives to identify endocrine disrupting chemicals (EDCs) and potential EDCs*. Nairobi: United Nations Environment Programme. [wedocs.unep.org/bitstreamhandle/20.500.11822/25633/EDC\\_report1.pdf?sequence=1&isAllowed=y](http://wedocs.unep.org/bitstreamhandle/20.500.11822/25633/EDC_report1.pdf?sequence=1&isAllowed=y). Accessed: 21 September 2022.
48. Brandsma S, Koekkoek J, Van Velzen M, *et al.* (2019) The PFOA substitute GenX detected in the environment near a fluoropolymer manufacturing plant in the Netherlands. *Chemosphere*, 220, 493–500. [doi.org/10.1016/j.chemosphere.2018.12.135](https://doi.org/10.1016/j.chemosphere.2018.12.135).
49. Wang Z, Cousins IT, Scheringer M, *et al.* (2015) Hazard assessment of fluorinated alternatives to long-chain perfluoroalkyl acids (PFAAs) and their precursors: status quo, ongoing challenges and possible solutions. *Environment International*, 75, 172–179. [doi.org/10.1016/j.envint.2014.11.013](https://doi.org/10.1016/j.envint.2014.11.013).
50. Hass U, Christiansen S, Andersson A-M, *et al.* (2019) *Report on Interpretation of knowledge on endocrine disrupting substances (EDs) – what is the risk?* Copenhagen: Danish Centre on Endocrine Disruptors (CeHoS). [www.cend.dk/files/ED\\_Risk\\_report-final-2019.pdf](http://www.cend.dk/files/ED_Risk_report-final-2019.pdf). Accessed: 16 September 2022.
51. Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal (1989). [www.basel.int/TheConvention/Overview/TextoftheConvention/tabid/1275/Default.aspx](http://www.basel.int/TheConvention/Overview/TextoftheConvention/tabid/1275/Default.aspx). Accessed: 21 September 2022.

52. Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (2019). [www.pic.int/TheConvention/Overview/TextoftheConvention/tabid/1048/language/en-US/Default.aspx.n-US/Default.aspx](http://www.pic.int/TheConvention/Overview/TextoftheConvention/tabid/1048/language/en-US/Default.aspx.n-US/Default.aspx). Accessed: 21 September 2022.
53. García Ibarra V, Rodríguez Bernaldo De Quirós A, Paseiro Losada P, *et al.* (2019) Non-target analysis of intentionally and non intentionally added substances from plastic packaging materials and their migration into food simulants. *Food Packaging and Shelf Life*, 21, 100325. [doi.org/10.1016/j.fpsl.2019.100325](https://doi.org/10.1016/j.fpsl.2019.100325).
54. Geueke B, Groh K, and Muncke J (2018) Food packaging in the circular economy: Overview of chemical safety aspects for commonly used materials. *Journal of Cleaner Production*, 193, 491–505. [doi.org/10.1016/j.jclepro.2018.05.005](https://doi.org/10.1016/j.jclepro.2018.05.005).
55. National Research Council (2014) *Review of the Environmental Protection Agency's State-of-the-Science evaluation of nonmonotonic dose-response relationships as they apply to endocrine disruptors*. Washington, DC: The National Academies Press. [nap.nationalacademies.org/catalog/18608/review-of-the-environmental-protection-agencys-state-of-the-science-evaluation-of-nonmonotonic-dose-response-relationships-as-they-apply-to-endocrine-disruptors](http://nap.nationalacademies.org/catalog/18608/review-of-the-environmental-protection-agencys-state-of-the-science-evaluation-of-nonmonotonic-dose-response-relationships-as-they-apply-to-endocrine-disruptors). Accessed: 21 September 2022.
56. European Chemicals Agency (n.d.) *Mapping exercise – Plastic additives initiative*. [echa.europa.eu/mapping-exercise-plastic-additives-initiative](http://echa.europa.eu/mapping-exercise-plastic-additives-initiative). Accessed: 6 February 2022.
57. Ougier E, Ganzleben C, Lecoq P, *et al.* (2021) Chemical prioritisation strategy in the European human biomonitoring initiative (HBM4EU) – development and results. *International Journal of Hygiene and Environmental Health*, 236, 113778. [doi.org/10.1016/j.ijheh.2021.113778](https://doi.org/10.1016/j.ijheh.2021.113778).
58. Hodgson R (2022) EU poised to restrict swathes of 'the most harmful chemicals'. *ENDS Europe*. [www.endseurope.com/article/1753914/eu-poised-restrict-swathes-the-harmful-chemicals](http://www.endseurope.com/article/1753914/eu-poised-restrict-swathes-the-harmful-chemicals). Accessed: 21 September 2022.
59. European Chemicals Agency (2018) *Strategy to promote substitution to safer chemicals through innovation: January 2018*. [data.europa.eu/doi/10.2823/99862](http://data.europa.eu/doi/10.2823/99862).
60. Organisation for Economic Co-operation and Development (n.d.) *Extended producer responsibility*. [www.oecd.org/environment/extended-producer-responsibility.htm](http://www.oecd.org/environment/extended-producer-responsibility.htm). Accessed: 1 August 2023.
61. Fletcher S, Roberts K, Shirian Y, *et al.* (2021) *Policy options to eliminate additional marine plastic litter by 2050 under the G20 Osaka Blue Ocean Vision: An international resource panel think piece*. Nairobi: United Nations Environment Programme. [circulareconomy.europa.eu/platform/sites/default/files/policy\\_options\\_to\\_eliminate\\_additional\\_marine\\_plastic\\_litter.pdf](http://circulareconomy.europa.eu/platform/sites/default/files/policy_options_to_eliminate_additional_marine_plastic_litter.pdf). Accessed: 10 February 2023.
62. International Chemical Secretariat (2021) *ChemSec SIN List – Substitute It Now*. [sinlist.chemsec.org/](http://sinlist.chemsec.org/). Accessed: 22 July 2021.
63. TCO Certified (n.d.) *TCO Certified Accepted Substance List*. [tcocertified.com/industry/accepted-substance-list/](http://tcocertified.com/industry/accepted-substance-list/). Accessed: 21 September 2022.
64. International Chemical Secretariat (2021) *ChemSec Marketplace*. [marketplace.chemsec.org](http://marketplace.chemsec.org). Accessed: 23 July 2021.
65. Organisation for Economic Cooperation and Development, and European Chemicals Agency (2022) *QSAR Toolbox*. [qsartoolbox.org](http://qsartoolbox.org). Accessed: 1 August 2022.
66. Apple Inc (2016) *Environmental responsibility report. 2016 progress report, covering fiscal year 2015*. Cupertino, CA. [www.apple.com/environment/pdf/Apple\\_Environmental\\_Responsibility\\_Report\\_2016.pdf](http://www.apple.com/environment/pdf/Apple_Environmental_Responsibility_Report_2016.pdf). Accessed: 14 September 2022.
67. Pecht MG, Ali I, and Carlson A (2017) Phthalates in electronics: the risks and the alternatives. *IEEE Access*, 6, 6232–6242. [doi.org/10.1109/ACCESS.2017.2778950](https://doi.org/10.1109/ACCESS.2017.2778950).

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