Research Paper

Implementing the EU Chemicals Strategy for Sustainability: The case of food contact chemicals of concern

Lisa Zimmermann a,⁎, Martin Scheringer b, Birgit Gueke a, Justin M. Boucher a, Lindsey V. Parkinson a, Ksenia J. Groh c, Jane Muncke a

a Food Packaging Forum Foundation, 8045 Zürich, Switzerland
b Department of Environmental Systems Science, ETH Zürich, 8092 Zürich, Switzerland
c Eawag, Swiss Federal Institute of Aquatic Science and Technology, 8600 Dübendorf, Switzerland

HIGHLIGHTS

• Food contact materials (FCMs) may contain 388 chemicals of concern (FCCoCs).
• According to the EU’s Chemicals Strategy, these FCCoCs should be phased out.
• For 127 of the FCCoCs, there is empirical evidence for their presence in FCMs.
• 352 FCCoCs are CMRs of which 85 have evidence for migration into foodstuff.
• Monomers, which are CMRs, can migrate from FCMs and are relevant for human exposure.

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ABSTRACT

The EU Chemicals Strategy for Sustainability (CSS) aims at removing the most harmful chemicals from consumer products, including from food contact materials (FCMs). If implemented as intended, the CSS has the potential to significantly improve the protection of public health by banning the use of chemicals of concern that are carcinogenic, mutagenic, or toxic to reproduction (CMRs), or persistent and bioaccumulative, or endocrine-disrupting chemicals (EDCs) in FCMs. However, until now an overview of such food contact chemicals of concern (FCCoCs) has not been available, because the CSS is fairly recent. Therefore, we here systematically analyze the food contact chemicals listed for intentional use in FCMs and identify known FCCoCs. We present a list of 388 FCCoCs that should be phased-out from use. Of these, 352 are CMRs, four are per- and polyfluoroalkyl substances (PFAS), and 127 have empirical evidence for presence in FCMs. Importantly, 30 FCCoCs with evidence for presence are monomers of which 22 have evidence for migration into foodstuff showing that monomers in FCMs indeed become relevant for human exposure. Our findings justify moving away from a risk- towards a hazard-based approach to regulation of chemicals in FCMs.

⁎ Corresponding author.
E-mail address: lisa.zimmermann@fp-forum.org (L. Zimmermann).

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1. Introduction

The European Union has expressed its intention to improve the protection of human health and reduce the use of hazardous chemicals, including in food contact materials (FCMs). This intention is stated in the EU’s Chemicals Strategy for Sustainability (CSS) (EC, 2020a) and in its Farm to Fork (F2F) strategy (EC, 2020b). Specifically, the CSS intends that consumer products do not contain the most harmful chemicals, which it defines as chemicals that are carcinogenic, mutagenic, or toxic to reproduction (CMRs), persistent and bioaccumulative, as well as endocrine-disrupting chemicals (EDGs). At a later stage, this approach might be extended to include further harmful chemicals such as substances that affect the immune, neurological, or respiratory system and chemicals toxic to a specific organ. The CSS further mentions ambitions to introduce persistent, mobile, and toxic (PMT), as well as very persistent, very mobile (vPvM) substances (i.e., chemicals with persistence- and mobility-related hazards) as categories of substances of very high concern (SVHCs) (EC, 2020a). SVHCs are substances with hazard properties requiring control, and as consequence, such SVHCs are to be phased-out and replaced by alternatives (ECHA, 2018). Here, we asked the question of which chemicals present in FCMs (i.e., food contact materials, FCCs) are known to have the above-mentioned hazard properties and hence should be flagged for phase-out according to the CSS.

There are thousands of FCCs: 12,285 chemicals have been identified for intentional use in the manufacturing of FCMs and food contact articles (FCAs) (Groh et al., 2021) and in addition there is a much higher number of non-intentionally added substances (NIAS) (Geueke, 2018). Contrary to the known intentionally added substances (IAS), such as additives and production aids, the NIAS include impurities (e.g., compounds present in the raw material such as lead, which is naturally present in silica sand used to produce glass), contaminants (e.g., cleaning agents, lubricants), breakdown products (e.g., degradation products of antioxidants such as nonylphenol), and reaction by-products (e.g., oligomers such as styrene oligomers). Many of these NIAS are essentially unknown. Altogether, up to 100,000 chemicals may be present in FCMs and transfer (i.e., migrate) from FCMs into food and beverages during processing, transport, storage, and food preparation (McCombie, 2018). Migration from FCAs into foodstuffs is common and results in human exposure to complex chemical mixtures (Muncke et al., 2020). Concerns have focused on a small subset of chemicals with well-researched and -described hazards, such as phthalates and bisphenols (Wagner, 2017; Wagner and Oehlmann, 2009). As a result, some of these substances have been addressed by specific regulations (e.g., restriction of phthalates; EU, 2018) and/or have been substituted by alternatives which, however, can be as harmful (e.g., bisphenol A by structurally similar bisphenols; Edaes and Souza, 2022; Trasande et al., 2021). But, there are many more chemicals with well-described hazard properties that have received much less attention.

Here, we introduce the term “food contact chemicals of concern” (FCCoCs) with which we refer to the FCCs with hazard properties defined by the CSS as “most harmful” (CMR chemicals, EDGs, chemicals with persistence-bioaccumulation-related hazards), “further harmful” (chemicals with specific target organ toxicity (STOT)) as well as chemicals mentioned to be introduced as SVHCs (chemicals with persistence-mobility-related hazards). Chemicals that are persistent and mobile can travel long distances in waterways and the atmosphere, leading to widespread environmental presence (Reemtsma et al., 2016). To date, there is no easily accessible and science-based overview of FCCoCs that may be used in the production of FCMs or FCAs. Therefore, here we perform a systematic identification of FCCoCs among the known intentionally used FCCs. We provide a list of the identified FCCoCs together with information on their hazards, uses, and production volumes. Furthermore, we perform four case studies to draw attention to selected groups of FCCoCs, exemplifying their hazards and uses. The first case study focuses on chemicals with analytical (i.e. empirical) evidence for presence in FCMs. These include chemicals shown to migrate into food or food simulants, i.e., FCCs directly relevant for human exposure, as well as FCCs detected in extracts, implying that they are present in FCMs. Three additional case studies address CMRs, monomers, and per- and polyfluoroalkyl substances (PFAS), respectively.

2. Methods

To extract the relevant information for compiling the Food Contact Chemicals of Concern (FCCoC) list, we consulted the data sources outlined below, which include several databases and chemical lists provided by government agencies (e.g., ECHA) or other organizations (e.g., Organisation for Economic Co-operation and Development, OECD).

2.1. Hazards and uses

We used the Food Contact Chemicals database’s (FCCdb) set of “priority hazardous substances” (Groh et al., 2021) as a basis to identify FCCoCs and their intentional uses. The FCCdb includes chemicals that have been identified by regulatory or industry inventories worldwide as potentially used in the manufacturing of FCMs and FCAs. Importantly, the FCCdb is a compilation of all known FCCs that may intentionally be used in FCMs and FCAs according to the 67 inventories that were consulted for the FCCdb compilation (see the FCCdb publication (Groh et al., 2021) for further information on the inventories). However, it is not known whether all of these FCCs are actually (still) used. We refer to these chemicals as intentionally added or intentionally used FCCs. In the FCCdb, we identified the chemicals that have been classified by official, publicly accessible sources (e.g., by the European Chemicals Agency (ECHA) or the US Environmental Protection Agency (EPA)) for at least one of the hazard properties mentioned in the CSS. These include CMRs, EDCs, STOT, chemicals with persistence-bioaccumulation-related hazards (i.e., persistent, bioaccumulative, and toxic (PBT) substances, very persistent and very bioaccumulative (vPvB) substances and/or persistent organic pollutants (POPs)) and chemicals with persistence-mobility-related hazards (i.e., PMT, vPvM) (Table 1). It has to be noted that for the substances that classify as CMRs based on the Globally Harmonized System (GHS) for classification and labeling, we only included those that are classified as category 1A (known) and category 1B (presumed) CMRs since they are most strictly regulated. Furthermore, we identified FCCoCs that are potential PMT or vPvM substances based on the German Environment Agency (UBA) report (126/2019), which systematically identifies PMT and vPvM substances among those registered under the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) regulation (Arp and Hale, 2019). In the FCCoC list, we only included the eight chemicals that the UBA had subjected to a detailed assessment and which are also on the FCCdb’s “prioritized hazardous substance” list. Moreover, chemicals with respiratory system hazards were not included since they are not considered relevant for FCMs, where chemical exposure is predominantly oral.

Data on the intentional use of FCCs are grouped into 16 FCM types: plastics, coatings, rubber, silicones, ion-exchange resins (IERs), paper & board, cellulose (regenerated cellulose), textiles, cork and wood, adhesives, colorants, printing inks, wax, “inorganic FCCs” (metals, glass, ceramics), active & intelligent materials, and “other uses.” This differs slightly from the 17 FCM types defined in the EU’s FCM Framework Regulation (EC) No 1935/2004 (EU, 2004). The FCM type “other uses” includes substances used in food contact applications other than in the production of FCAs, such as food processing operations (e.g., lubricants).

2.2. Chemical production volume

Data on chemical production volume were retrieved in October 2021 from ECHA’s Registered Substances List (ECHA, 2022d). We included information on whether a substance has or has not been registered under the REACH regulation, and for registered substances we also included the total tonnage registered in the EU. In addition, we screened the US
The EPA HPV list (HPV) for the FCCoCs identified and indicated whether an FCCoC is considered HPV when manufactured in or imported into the US in amounts of one million pounds (corresponding to 453.60 metric tons) or more per year.

### 2.3. Evidence for presence in FCMs

To retrieve information on the presence of the FCCoCs in FCMs, we used the Database on Migrating and Extractable Food Contact Chemicals (FCCmigex) (Geueke et al., 2022). The FCCmigex lists chemicals that have been measured analytically and detected either in migration experiments or in extracts of FCMs as reported by the scientific studies referenced in the database. Thereby, we define “migration” as “transfer of an FCC from an FCM or FCA into food or food simulants. Migration of an FCC into food may lead to human exposure after food consumption. Migration reflects realistic, intended-use and foreseeable conditions” (Martin et al., 2018). “Food” includes all types of foods and beverages that are suitable for human consumption, whereas “food simulants” serve as standardized surrogates for food or beverages. We define “extraction” as “transfer of an FCC from an FCM or FCA into a solvent when the conditions are chosen in such a way as to promote a strong interaction with an FCM, often resulting in a quicker mass transfer and equal or even exaggerated extents of migration. Extraction is defined as worst-case migration and reflects non-foreseeable use conditions” (Martin et al., 2018). The FCCmigex also contains analytical data from physical extraction experiments such as direct desorption from an FCA surface.

### 2.4. Monomers

To identify the FCCoCs that are used as monomers, we compared the Chemical Abstracts Service (CAS) numbers of the FCCoCs with evidence for presence in FCMs with Annex I of the Commission Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food (Union List) downloaded in November 2021 (EU, 2011). In addition, we compared the CAS numbers with the PlasticMAP database that identifies plastic monomers, additives, and processing aids (Wiesinger et al., 2021).

### 2.5. Per- and polyfluoroalkyl substances (PFAS)

To identify PFAS among the FCCoCs, we compared the CAS numbers of all FCCoCs with the OECD’s List of PFAS comprising 4730 PFAS in November 2021 (Wang, 2018).

### 3. Results

#### 3.1. FCCoCs used to manufacture FCMs and FCAs

We identified 388 chemicals that are listed for intentional use in FCMs according to the FCCdb (Groh et al., 2021) and are harmful according to the CSS due to their hazard properties of high concern (EC, 2020a). These 388 FCCoCs include 352 CMRs, 22 EDCs, three chemicals with STOT hazards, 32 with persistence- and bioaccumulation-related hazards (PBT, vPvB, POP), and eight with persistence- and mobility-related hazards (PMT, vPvM) (Fig. 1). Some of the FCCoCs have been classified for more than one hazard. For instance, eight of the EDCs and ten of the substances with persistence-bioaccumulation-related hazards are also CMRs (Table S1).

The highest number of FCCoCs may be intentionally used in printing inks (238 substances), followed by plastics (197), and paper & board (168) (Fig. 2). The majority of FCCoCs are used in more than one FCM type. For instance, 96 FCCoCs are listed for use in the manufacturing of five or more FCM types according to the FCCdb.

As of October 2021, 70 of the FCCoCs were registered under REACH in the EU, and 253 were included in the US EPA HPV list with an overlap of 50 chemicals being both REACH registered and on the EPA HPV list (Fig. 1). For 24 of the REACH-registered substances, the total tonnage band registered in the EU is $\geq 1000$ metric tons. Of these 24, diethanolamine (CAS 111–42–2), alpha-methylstyrene (CAS 98–83–9), bisphenol A (CAS 80–05–7), 1,3,5-trioxane (CAS 110–88–3), epichlorohydrin (CAS 106–89–8), and 1,2-dichloroethane (CAS 107–06–2) are registered with $\geq 100,000$ metric tons (Table S1).

#### 3.2. Case studies

To demonstrate the importance of phasing out the use of these 388 FCCoCs in FCMs, we evaluate in detail four subgroups of FCCoCs.

##### 3.2.1. FCCoCs with evidence for presence in FCAs

We compared the FCCoCs list with the FCCmigex (Geueke et al., 2022).
DNA, or damage reproductive systems. According to EU legislation, CMRs are the most toxic class of hazardous chemicals. Concerningly, three have persistence-mobility-related hazards, and one is classified as STOT, specific target organ toxicity after repeated exposure.

Fig. 1. Overview of the FCCoCs, their hazards, uses, and production volumes in the EU, according to the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) regulation, and in the US, according to the Environmental Protection Agency’s (EPA) High Production Volume (HPV) list. All these FCCoCs are identified for intentional use in food contact material (FCM) or food contact article (FCA) manufacturing according to the Food Contact Chemicals database (FCCdb, in grey), and for a subset there is evidence for presence in FCMs/FCAs according to the Database on Migrating and Extractable Food Contact Chemicals (FCCmigex, in orange). For more details see the Supplementary Material, and Table S1 “Read me”. CMR, carcinogenic, mutagenic, or toxic to reproduction; EDC, endocrine-disrupting chemical; STOT, specific target organ toxicity after repeated exposure.

We found that 30 of the FCCoCs are not only listed for intentional use in FCMs or have been detected analytically in migrants or extracts of FCMs, or both in migrants and in extracts of FCMs. This comparison showed that for 127 of the FCCoCs, there is empirical evidence for their presence in FCMs (Table S2). The detection in extracts indicates that a chemical is contained in an FCM, while the detection in migrants indicates that a chemical transfers into food under normal conditions of FCM use, and it is therefore relevant for human exposure via foodstuff. In total, 97 substances have been found to migrate from FCMs. This includes 57 chemicals with evidence for migration into food and 89 with evidence for migration into food simulants (Fig. 1).

Of the 127 FCCoCs with evidence for presence in FCMs, 112 are CMRs, 13 are EDCs, 16 have persistence-bioaccumulation-related hazards, three have persistence-mobility-related hazards, and one is classified as STOT (Fig. 1, Table S2).

3.2.2. CMRs
CMR chemicals have inherent properties that can cause cancer, alter DNA, or damage reproductive systems. According to EU legislation, CMRs are the most toxic class of hazardous chemicals. Concerningly, 352 of the identified FCCoCs are CMRs. Of these, 274 received a GHS-aligned CMR category 1 classification (by ECHA or the Japanese Government) or are on the Candidate List of SVHC for Authorization maintained under the REACH regulation (Table S3), while 175 chemicals are on California’s Office of Environmental Health Hazard Assessment’s (OEHHA) Proposition 65 List. 97 chemicals classify as CMRs based on both GHS/REACH SVHC and the Proposition List 65. The Proposition List 65 compiles chemicals known to cause cancer, birth defects, or other reproductive harm including “developmental toxicity”, “female reproductive toxicity”, and “male reproductive toxicity” (OEHHA, 1993). Of the CMRs classified by ECHA in alignment with the GHS, 18 and 117 received the hazard category carcinogenicity (carc.) 1A (known carcinogen) and 1B (presumed), respectively. For germ cell mutagenicity (muta.), the corresponding numbers are 0 for known, and 37 for presumed mutagens, whereas for reproductive toxicity (repr.) three were classified as known and 56 as presumed repr. chemicals (Table S3).

A wide variety of CMRs is listed for use in the manufacturing of printing inks (210 substances), plastics (179), paper & board (156), coatings (129), and rubbers (116) (Fig. 3). For around one-third (122) of the CMRs, there is evidence for presence in FCMs, and 85 of these CMRs have been found to migrate into food or food simulants, becoming available for human consumption (Fig. 2). The CMR chemicals listed for intentional use in the highest variety of FCM types are: formaldehyde (CAS 50–00–0) possibly used in 14 FCM types, styrene (CAS 100–42–5) and vinyl chloride (CAS 75–01–4) possibly used in 12 FCM types each, and acrylonitrile (CAS 107–13–1) and sodium tetraborate (CAS 1330–43–4) possibly used in 11 FCM types each (Table 2).

3.2.3. Monomers
Polymerization reactions are rarely complete and therefore residual monomers might still be present in plastics and other polymerized FCMs like printing inks, adhesives, or coatings. Dependent on the polymer type, the polymerization process, and the technique used for reducing residual monomer content, monomers can still account for up to 4% by weight in the final material (i.e., 40,000 ppm) (Araújo et al., 2002). Thus, we were interested in whether the FCCoC list includes monomers with empirical evidence for presence in FCMs, i.e., that are included in the FCCmigex database (Geueke et al., 2022). We found that 30 of the FCCoCs are monomers that have been analytically detected in FCMs. Among the 30 monomers included in the FCCoC list are well-known plastic monomers such as acrylamide (CAS 79–06–1), which is polymerized to polyacrylamide, styrene (CAS...
3.2.4. Per- and polyfluoroalkyl substances (PFAS)

PFAS are a class of several thousand chemicals with widespread use in different food contact applications, such as non-stick cookware, and grease-resistant food packaging (Glüge et al., 2020). Together with their very high environmental persistence, this widespread use has led to pervasive environmental contamination with PFAS (Rankin et al., 2016). PFAS have been detected in humans (Awad et al., 2020) and linked to diverse health issues (Pelich et al., 2021). We identified four PFAS when screening the 388 FCCoCs against the OECD’s list of PFAS (Wang, 2018); perfluorooctanoic acid (PFOA, CAS 335–67–1), the PFOA salt ammonium perfluorooctanoate (CAS 3825–26–1), bis(2-hydroxyethyl)ammonium perfluorooctanesulfonate (CAS 70225–14–8), and tetraethylammonium perfluorooctanesulfonate (CAS 56773–42–3) (Table 3, S5). These PFAS have been recognized for their persistence-bioaccumulation-related hazards. In addition, three of the four are also CMRs, while tetraethylammonium perfluorooctanesulfonate has potential persistence-mobility-related hazards. These PFAS have been listed for use in printing inks, plastics and/or coatings. Several scientific studies have found PFOA to migrate from different types of FCMs into food and food simulants (Choi et al., 2018; Sanchis et al., 2019; Timshina et al., 2021; Zabaleta et al., 2020).
Table 2

CMR chemicals listed for intentional use in ten or more FCM types. These chemicals also correspond to the ‘monomers with evidence for presence’ listed for intentional use in ten or more FCM types with the exception of sodium tetraborate and silicon dioxide (marked with *). IERs, ion-exchange resins; A&I, active & intelligent; Carc, carcinogenic; Muta, mutagenic; Reptr, toxic to reproduction.

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS</th>
<th>ECHA CMR hazard category</th>
<th>FCMs intentionally used in</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde</td>
<td>50–00–0</td>
<td>Carc.1B, Muta. 2</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, cellophane, textiles, cork and wood, adhesive, colorants, printing inks, wax, A &amp; I</td>
<td>14</td>
</tr>
<tr>
<td>Styrene</td>
<td>100–42–5</td>
<td>Repr. 2</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, textiles, adhesive, printing inks, wax, A &amp; I, other – flavoring substance</td>
<td>12</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>75–01–4</td>
<td>Carc. I A</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, cellophane, cork and wood, adhesive, colorants, printing inks, A &amp; I</td>
<td>12</td>
</tr>
<tr>
<td>Acrylonitrile</td>
<td>107–13–1</td>
<td>Carc. 1B</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, cellophane, textiles, cork and wood, adhesive, printing inks</td>
<td>11</td>
</tr>
<tr>
<td>Sodium tetraborate*</td>
<td>1330–43–4</td>
<td>Repr. 1B</td>
<td>Plastics, coatings, rubber, IER, paper/board, textiles, cork and wood, adhesive, printing inks, inorganics, A &amp; I</td>
<td>11</td>
</tr>
<tr>
<td>Bisphenol A</td>
<td>80–05–7</td>
<td>Repr. 2</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, adhesive, printing inks, inorganics, A &amp; I</td>
<td>10</td>
</tr>
<tr>
<td>Silicon dioxide*</td>
<td>7631–86–9</td>
<td>– (classified by Japan as Carc. 1A)</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, adhesive, printing inks, inorganics, A &amp; I</td>
<td>10</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>106–89–8</td>
<td>Carc. 1B</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, textiles, adhesive, printing inks, A &amp; I</td>
<td>10</td>
</tr>
<tr>
<td>Boric acid</td>
<td>10043–35–3</td>
<td>Repr. 1B</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, textiles, cork and wood, adhesive, printing inks</td>
<td>10</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>140–88–5</td>
<td>– (on Prop 65 list)</td>
<td>Plastics, coatings, rubber, silicones, IER, paper/board, cellophane, adhesive, printing inks, other (flavoring substance)</td>
<td>10</td>
</tr>
<tr>
<td>1,1-Dichloroethylene</td>
<td>75–35–4</td>
<td>– (on Prop 65 list)</td>
<td>Plastics, coatings, rubber, IER, paper/board, cellophane, cork and wood, adhesive, printing inks</td>
<td>10</td>
</tr>
</tbody>
</table>

acknowledge that this information would be relevant. Furthermore, data on FCCs are constantly updated so that some information (e.g., hazard classifications, uses of a chemical) may have changed since the analyzed data were collected.

4.2. Utilizing the FCCoC list when implementing the EU Chemicals Strategy

From an EU regulatory perspective, the identified FCCoCs should no longer be permitted for intentional use in FCMs. According to the Farm-to-Fork strategy, which is at the heart of the European Green Deal, “the Commission will revise the food contact materials legislation to improve food safety and public health (in particular in reducing the use of hazardous chemicals)” (EC, 2020b). In addition, the CSS clearly states the ambition that consumer products, including FCMs, toys, and childcare articles, “do not contain chemicals that cause cancers, gene mutations, affect the reproductive or the endocrine system, or are persistent and bioaccumulative. In addition, [the Commission will] immediately launch a comprehensive impact assessment to define the modalities and timing for extending the same generic approach, with regard to consumer products, to further harmful chemicals, including those affecting the immune, neurological or respiratory systems and chemicals toxic to a specific organ” (EC, 2020a). All chemicals included in the FCCoC list have at least one of the outlined hazard properties or shall be introduced as SVHC category (i.e., PMT and vPvM substances) according to the CSS.

One approach for excluding the use of these FCCoCs in FCMs is to consider them during the European Commission’s currently ongoing revision of the EU’s FCM regulation (EC, 2020a; EU, 2004), for example in the form of a regularly updated negative list of chemicals that are not permitted for use in any FCM. Further, the elimination of chemicals known to harm human health supports European ambitions towards material circularity, including increased food packaging recycling rates, since known hazardous chemicals would then not be used in virgin materials and therefore not perpetuated in recycled packaging material (EC, 2018; Geuseke et al., 2018).

The CSS also mentions explicitly that toys and childcare articles should not contain chemicals with the above-mentioned hazards (EC, 2020a). Currently, toy safety is regulated by Directive 2009/48/EC (Toy Safety Directive) (EU, 2009), which lays out that CMRs shall not be used in toys. However, only a few chemicals are specifically regulated (listed in Appendix C to Annex II) while the remaining CMRs might still be present in toys as long as their concentration is below the concentration to which they were classified as CMRs according to the CLP regulation (EC) No. 1272/2008 (EU, 2008). These maximum concentrations were, however, not derived by toxicological risk assessments. Eliminating CMRs from all FCMs, including those intended for infants and children, as well as from toys and childcare articles will improve protection of this sensitive population group.

Importantly, even FCCoCs with Specific Migration Limits (SML), as they are detailed in the EU Plastic FCM regulation (EU, 2011), have been found to transfer into food at levels above their SML. Acrylamide (CAS 79–06–1) (RASFF, 2021b), bisphenol A (CAS 80–05–7) (RASFF, 2022), and formaldehyde (CAS 50–00–0) (RASFF, 2021a, 2021c), for instance, were detected in food or beverages on the European market at levels above their SML according to notification of RASFF – the Rapid Alert System for Food and Feed. For other FCCoCs, the SMLs have been lowered over the years with emerging hazard data, for example in the case of BPA (CAS 80–05–7). Indeed, a recent draft Scientific Opinion from the European Food Safety Authority (EFSA) proposes to yet further lower the tolerable daily intake (TDI) of BPA by a factor of 100 000 based on its health hazard (EFSA, 2021). This in turn implies that the SML for BPA would need to be lowered from currently 50 µg/kg food to 2.4 ng/kg food (or lower to account for other, non-FCM exposure sources) – a limit that is likely too low to be enforceable. As consequence, a total ban of BPA use in FCMs appears to be inevitable.

The fact that chemicals are currently present in FCMs above their legal limits shows that the enforceability of regulations needs to be improved and compliance with regulations needs to be increasingly checked. The harmonization of national and EU regulations on FCMs as well as REACH can help here (Daniel et al., 2019; Grob, 2019; Pawlicka et al., 2020). In addition, there is a need to guarantee that products imported to the EU do not contain banned chemicals or substances other than those explicitly approved in the EU. The priority FCCoC list presented here can contribute to compliance checks by authorities through providing information on which FCM types likely contain certain FCCoCs.

Furthermore, legal limits may be founded on outdated hazard data. For instance, Maffini et al. (2021) reviewed human health effects...
associated with the exposure to certain phthalates and concluded that existing safe levels of exposure (e.g., reference doses) may not be sufficiently protective. This demonstrates the necessity to re-evaluate FCCs. Existing safe levels of exposure (e.g., reference doses) may not be sufficiently protective. This demonstrates the necessity to re-evaluate FCCs.

The four PFAS included in the FCCoC list.

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS</th>
<th>Hazards</th>
<th>FCM types intentionally used in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfluorooctanoic acid (PFOA)</td>
<td>335–67–1</td>
<td>CMR, persistence-bioaccumulation (PBT and POP)</td>
<td>Plastics, coatings</td>
</tr>
<tr>
<td>Ammonium perfluorooctanoate (PFOA salt)</td>
<td>3825–26–1</td>
<td>CMR, persistence-bioaccumulation (PBT)</td>
<td>Plastics, coatings, printing inks</td>
</tr>
<tr>
<td>Bis(2-hydroxyethyl)ammonium perfluorooctanesulfonate</td>
<td>70225–14–8</td>
<td>CMR, persistence-bioaccumulation (POP)</td>
<td>Printing inks</td>
</tr>
<tr>
<td>Tetraethylammonium perfluorooctanesulfonate</td>
<td>56773–42–3</td>
<td>Persistence-bioaccumulation (PBT/vPvB), persistence-mobility (vPvM, PMT)</td>
<td>Printing inks</td>
</tr>
</tbody>
</table>

Table 3: The four PFAS included in the FCCoC list.

4.3. Case studies - insights into the FCCoCs

4.3.1. FCCoCs with evidence for presence in FCAs

For 127 of the FCCoCs, there is empirical evidence of their presence in FCAs (Fig. 1). Moreover, 97 of the 127 chemicals have been found to transfer from FCIs into food, food simulants, or both. This demonstrates that numerous chemicals with well-described hazard properties of high concern transfer into food under normal conditions of use. This allows for investigating whether they are actually in use and whether they transfer from FCIs into food or into food simulants under realistic conditions of use. Furthermore, some of the 127 FCCoCs with evidence for presence were only targeted in extraction and not in migration experiments. Analyzing also the migration of these chemicals would help to clarify their relevance for human exposure via foodstuffs.

4.3.2. CMRs

Our study shows that a wide variety of CMRs is potentially used in food packaging. 352 CMRs have been listed for use in the manufacturing of FCIs. Of these, 135 were classified by ECHA as category 1 carcinogens, which recognizes them as known or presumed human carcinogens based on evidence from humans or well-performed animal studies. Among these FCCoCs are for instance the monomers vinyl chloride (CAS 75–01–4) and 1,2-dichloroethane (CAS 107–06–2), both of which are used for PVC production, styrene oxide used as a plasticizer or diluent for epoxy resins (CAS 96–09–3), and 5-methyl-o-anisidine (CAS 120–71–8) used in the manufacturing of dyes. Another CMR listed for use in more than ten FCIs is epichlorohydrin (CAS 106–89–8; Table 2), which is used as monomer for epoxy resin production but also listed for intentional use in several other FCIs including textiles, adhesives, and printing inks. Epichlorohydrin is a presumed carcinogen (carr 1B), which has a total tonnage band registered under REACH in the EU of 100,000 to 1,000,000 metric tons.

Moreover, our data demonstrate that 122 CMRs have been analytically detected to be present in FCIs, and 85 of these were shown to migrate into food or food simulants under normal conditions of use. This means that humans are likely directly exposed through food to CMRs originating from food packaging and other FCIs. Considering the increasing prevalence of cancers and other chronic diseases in the human population that are associated with hazardous chemical exposures (e.g., infertility, diabetes), this entirely avoidable exposure source to hazardous chemicals urgently needs to be addressed. The presence of CMRs in FCIs is even more troubling since the entire human population, including the most sensitive population groups (e.g., unborn, children, chronically ill) are ubiquitously exposed to these chemicals daily.

Importantly, many more CMRs are potentially added to FCIs. For instance, in the FCCoC list we only included the chemicals that received a GHS-aligned category 1 CMR classification leaving aside all the category 2 CMRs. We only focused on category 1 CMRs since they are most strictly regulated. As an example, the generic limits of CMRs in toys correspond to the concentration to which they were classified as CMRs according to the CLP Regulation (ECHA, 2022a), which usually means a concentration of up to 0.1% (0.3% for those toxic to reproduction) for category 1A and 1B CMRs while it is 1% (3% for rep. 2) for category 2 CMRs. Alone 86 chemicals included in the FCCdb have been classified by ECHA as carc. 2 (Groh et al., 2021), demonstrating the wide scale of category 2 CMRs’ intentionally use in FCIs. Furthermore, category 2 CMRs may eventually be re-classified to category 1 substances when more hazard data become available. And, what is more, from the CSS text we could not identify whether the EU Commission intends to cover both, category 1 and category 2 CMRs (EC, 2020a). However, eventually also category 2 CMRs should be phased out from intentional use in FCIs due to their high level of concern.

4.3.3. Monomers

We identified 30 monomers of concern for which there is empirical evidence for presence in FCIs, based on migration and/or extraction experiments (Fig. 2). Monomers serve as starting material for manufacturing polymers, which are used for example in plastics, adhesives, and coatings. Monomers known to be hazardous are allowed for polymer production for FCIs, based on the assumption that they are chemically transformed into polymers and that the molecular weight of...
the resulting polymers is too high for the polymers to be taken up in the gastro-intestinal tract, enter cells, and induce toxic effects (Groh et al., 2017; Silano et al., 2008).

However, as our data demonstrate, unreacted monomers are still present in polymeric materials of finished FCMs. The presence of these monomers can either indicate that (i) unpolymerized monomers are still contained in the final article, underscoring that polymerization reactions are rarely complete, (ii) that the respective chemical was not used as a monomer but to serve another purpose, or (iii) that the polymer is degrading and there is a release of the monomer (e.g. in the case of polycarbonate). Examples of dual use of a chemical as a monomer and additive include: 1,4-dichlorobenzene (CAS 106–46–7) used as a precursor of the polymer poly(p-phenylene sulfide) but also as an odor agent or plasticizer, as well as ethylene glycol (CAS 07–21–1) and epichlorohydrin (CAS 106–89–8), which are used as a precursor of polyesters and of epoxy resins, respectively, but both also as cross-linking agents, light stabilizers, and lubricants (Wiesinger et al., 2021).

Furthermore, empirical data show that monomers with known hazard properties concern also transfer into foodstuff under realistic conditions: 22 of the FCCoC monomers have been shown to migrate into food or food simulant (Fig. 2). This demonstrates that the assumption of these monomers do not migrate under actual conditions of use is factually not correct.

Importantly, monomers most often are highly reactive substances, which implies that they are likely to be highly hazardous chemicals. This is demonstrated by our data showing that 20 of the 22 migrating monomers were classified as CMRs according to EU REACH SVHC- or GSH-criteria (category 1 CMRs) and/or the criteria of the US Proposition 65 list (Table S4). Among them are monomers for which the levels migrating into food must be below the limit of detection or below 10 µg/kg food, according to Annex I of Regulation (EU) No.10/2022 (EU, 2011), including vinyl chloride (CAS 75–01–4), acrylonitrile (CAS 107–13–1), and 1,3-butadiene (CAS 106–99–0). This shows that monomers that are known (1A) or presumed (1B) carcinogens and are not supposed to transfer from plastic FCMs nevertheless do migrate from FCMs. Moreover, a migration threshold for known CMRs of 10 µg/kg food is neither based on human health considerations (Muncke et al., 2017) nor is it aligned with the call for a ban of such substances as expressed in the EU’s CSS and the F2F strategy.

One monomer with evidence for migration and of particular concern included in the FCCoC list is styrene. The 15th Report on Carcinogens of the National Toxicology Program finds styrene “reasonably anticipated to be a human carcinogen” (NTP, 2021), and ECHA classifies it as a suspected human reproductive toxicant (rep 2; Table S4), but despite this it is still being intentionally used in 14 FCM types (Table S4). For the use of styrene in plastic FCMs, no SML exists (EU, 2011). Therefore, it is not surprising that scientific evidence for the migration of styrene into food is widespread (Table S4; Sadighara et al., 2022).

As outlined, our study clearly demonstrates that FCMs can contain unpolymerized residues of several monomers of high concern that can transfer into food, thereby exposing the human population via this avoidable source. Recognizing this fact is the first but very important step to move forward towards safer FCMs.

4.3.4. PFAS

Among the FCCoCs are four PFAS that all have persistence-bioaccumulation-related hazards; three have also been classified as CMRs. Empirical data show that PFOA migrates from several FCMs into food and food simulants, and it is therefore directly relevant for human exposure (Table S4). With the addition of PFOA (and its salts) to the Stockholm Convention in 2019, its production and use is forbidden (Stockholm Convention, 2017). Nevertheless, there have since been studies published reporting the presence of PFOA in FCMs (Greece et al., 2022). This indicates that PFOA is still being intentionally used in FCMs, that the FCAs it was detected in were produced before 2019, or that PFOA is present as an unintentional contaminant, for example as an impurity from the manufacturing process. To identify the origins of detected PFOA and guarantee that FCMs are free of it, further investigation and enforcement are needed.

Especially concerning is that several dozen additional PFAS are included within the FCCmigex for their evidence of presence in FCMs (Greece et al., 2022) but not included in the FCCdb (Groh et al., 2021), owing to a lack of public information about their intentional use. These substances are therefore also not in the FCCoC list presented here. However, some of these additional and detected PFAS have been reported to have hazard properties of high concern including perfluorohexanoic acid (PFHxA, CAS 307–24–4) and related salts (US EPA, 2022), perfluorohexanesulfonic acid (PFHxS, CAS 355–46–4), 6:2 fluoroalterolomer alcohol (FTOH, CAS 647–42–7), and perfluoro (2-methyl-3-oxahexanoic) acid (GenX, CAS 13252–13–6) (Temkin et al., 2020). On a general level, this highlights that there are many more (potentially harmful) chemicals, including PFAS, that are not included in governmental or industry inventories for FCMs but could nevertheless be present in materials on the market. With the shift across the chemicals sector from longer chain to shorter chain PFAS over the past decade (Boucher et al., 2019; Wang et al., 2017), many novel PFAS are thought to have been developed and increasingly used as replacements for PFOS and PFOA, across a wide range of products. Barhoumi et al. (2021) performed a systematic review and found that a wide variety of anionic and non-ionic PFAS are contained in FCMs. These include perfluoroalkyl acids (PFAs) and their precursors in concentrations varying among countries due to the different formulations used and legislations applied (Barhoumi et al., 2021). Accordingly, it would be desirable to regularly update the FCCdb to ensure it reflects the substances on the market, and the planning for this work is in progress.

Given the lack of information in the public domain about the current intentional uses of PFAS in FCMs, especially novel PFAS, as well as widespread concerns about their hazard properties, further scientific research and policy efforts are needed to close these data gaps and implement steps where needed to address safety concerns. In this regard, the ongoing efforts of EU Member States for a general PFAS ban are important (RIVM, 2021).

4.4. The way forward: identification of FCCoC sources and options for reducing exposure

Why are FCCoCs still allowed for use in FCMs and how can this issue be resolved? According to the European Regulation (EC) No. 1935/2004 for materials and articles intended to come into contact with food, FCMs shall be manufactured so that “under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities which could endanger human health” (EU, 2004). For CMRs, this implies that they should not transfer into food at all since there is an agreement that no safe levels for exposure to CMRs exist. However, as we show here, 112 chemicals with known CMR properties have evidence for presence in FCMs of which 85 were found to migrate from FCMs into food or food simulants. Thus, the current regulatory approach does not ensure that CMRs and other FCCoCs only transfer at truly “safe levels”. In addition, determining these thresholds for all chemicals used in FCMs is empirically not possible, both due to the low levels causing harm and also because of the large number of FCCs used, which is estimated to be over 12,285 (Groh et al., 2021). Indeed, most chemicals currently in use, including FCCs, cannot be properly risk assessed, risk managed, and enforced (Fenner and Scheringer, 2021; Muncke et al., 2017; Simonneau and Hoekstra, 2016). For these reasons, the regulatory definition of safety needs to be adjusted to better reflect the reality. This means that FCM safety should be redefined to mean that no untested substances and no hazardous chemicals are present in a finished FCA.

To better protect human health, we strongly support the ambition of the CSS to move away from the current risk-based approach, which considers human exposure levels in addition to a chemical’s hazard, and
towards a hazard-based approach (also called Generic Risk Assessment). In this approach, the use of a known hazardous chemical is not authorized for FCM manufacture, and the presence of a potentially hazardous chemical at detectable levels in food or food simulants is used for risk management activities. For example, Lithner et al. (2011) performed a hazard ranking of polymers by looking at the hazard classification of the underlying monomers, and they found 16 of the 55 assessed polymers to consist of monomers that are classified as CMRs category 1A or 1B. Following a hazard-based approach, these monomers should be eliminated from use. Three of these monomers (acrylonitrile, methacryloxy-drin, and vinyl chloride) correspond to the monomers included in Table 2 with intentional use in the highest variety of FCM types.

Some alternatives to the FCCoCs identified in this paper that fulfill the same function have already been suggested. For instance, a report by the OECD summarizes that commercially available non-fluorinated alternatives to long-chain PFAS in paper and paperboard food packaging share the same grease- and water-repellent performance (OECD, 2020).

Further, instead of substituting individual chemicals, also a whole packaging material may be substituted with a safer alternative. As an example, by substituting plastics with stainless steel or glass packaging, a material of higher inertness is used, i.e., a material with lower chemical migration and absorption. Science-based tools, such as the Understanding Packaging (UP) Scorecard (Single-Use Material Decr- erator (SUMD), 2022), can help to compare different food packaging options with regard to chemicals of concern and different sustainability indicators (e.g., climate, water use) to help the user to make informed decisions. However, hazard data for FCCs are generally lacking or outdated, which restricts the identification of truly safe chemicals and products. Furthermore, substituting chemicals (or even products) of concern one by one with potentially safer alternatives takes a lot of time and resources. Therefore, more efficient approaches need to be worked out and implemented to address the development of safer alternatives for use in FCMs. As one step in that direction, the essential-use concept (EUC) has been proposed to accelerate the phase-out of substances of concern such as PFAS (Cousins et al., 2019). The applicability and effectiveness of the EUC have been outlined in detail and exemplified elsewhere (Cousins et al., 2021). It aims to identify uses of substances of concern that can be phased out with the highest priority and without detailed risk assessments. Eventually, a combination of several strategies is needed to approach the FCCoCs issue. One aim should be the reduction of food packaging in general. This can be achieved by initiating structural changes (e.g., producing and selling food locally making transport packaging superfluous), behavioral changes, (e.g., purchasing fresh and seasonal food), and mindset changes (e.g., moving away from the idea that all food must be available at all times and locations). In cases where food packaging is needed, regulatory reform (e.g., hazard-based approach, adoption of safety definition) combined with a higher incentive for product manufacturers to design safer FCCs and FCMs, are two key components to reducing exposure to FCCoCs.

4.5. Conclusions

Here, we provide an overview of FCCs that are of concern according to the CSS. The developed FCCoC list was rigorously compiled in a systematic, transparent, and scientific way. Chemicals included in the FCCoC list should be considered for immediate phase-out from intentional use in FCMs, and finished FCAs should be screened for FCCoCs that may be present non-intentionally.

Regulatory reform is essential to guarantee the safety of FCMS and FCAs: The revision of the EU FCM Framework Regulation (EU, 2004) needs to address the reality that FCMs are currently chemically too complex for a reliable exclusion of FCCoCs. This revision should aim to (i) reduce the number of authorized substances for FCM manufacture, reduce the overall diversity of chemicals used, and provide a list of safer chemicals (“positive list”), (ii) include a list of substances that are explicitly not authorized for use due to their inherent hazard properties (“negative list”), and (iii) redefine the concept of “safety” for FCCs to move away from the scientifically disproven paradigm of safe levels (“the dose makes the poison”) towards Generic Risk Assessment.

Environmental implication

Our study demonstrates that several hundred chemicals with well-known hazard properties of highest concern (e.g., CMR, persistent, bioaccumulative, mobile substances) are intentionally used in food contact materials (FCMs), making FCMs “hazardous materials”. These chemicals can migrate into food (e.g., during transportation and storage) as well as in the environment (e.g., when improperly disposed) becoming relevant for the exposure of humans and other organisms. Especially persistent, bioaccumulative, and mobile substances can have long-term and widespread environmental consequences. Our overview of chemicals of concern in FCMs can assist regulators, product manufacturers, and researchers in developing safer materials.

CRediT authorship contribution statement

JM, MS, and LZ conceptualized the paper and wrote the manuscript. LZ and LVP compiled and processed the data. KG provided her expertise in FCCoC hazard assessment and monomer identification. All authors proofread the manuscript and provided constructive input.

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Competing interests

The authors declare no conflicts of interest. LZ, BG, JMB, LVP, and JM are employees of the Food Packaging Forum (FPF) Foundation, an independent and charitable foundation dedicated to science communication and research on chemicals in all types of food contact materials and articles. KS and MS are members of FPF’s scientific advisory board and MS also of FPF’s foundation board, but they are not remunerated for this role.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2022.129167.

References


