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Supplemental Material

Scientific Challenges in the Risk Assessment of Food Contact Materials

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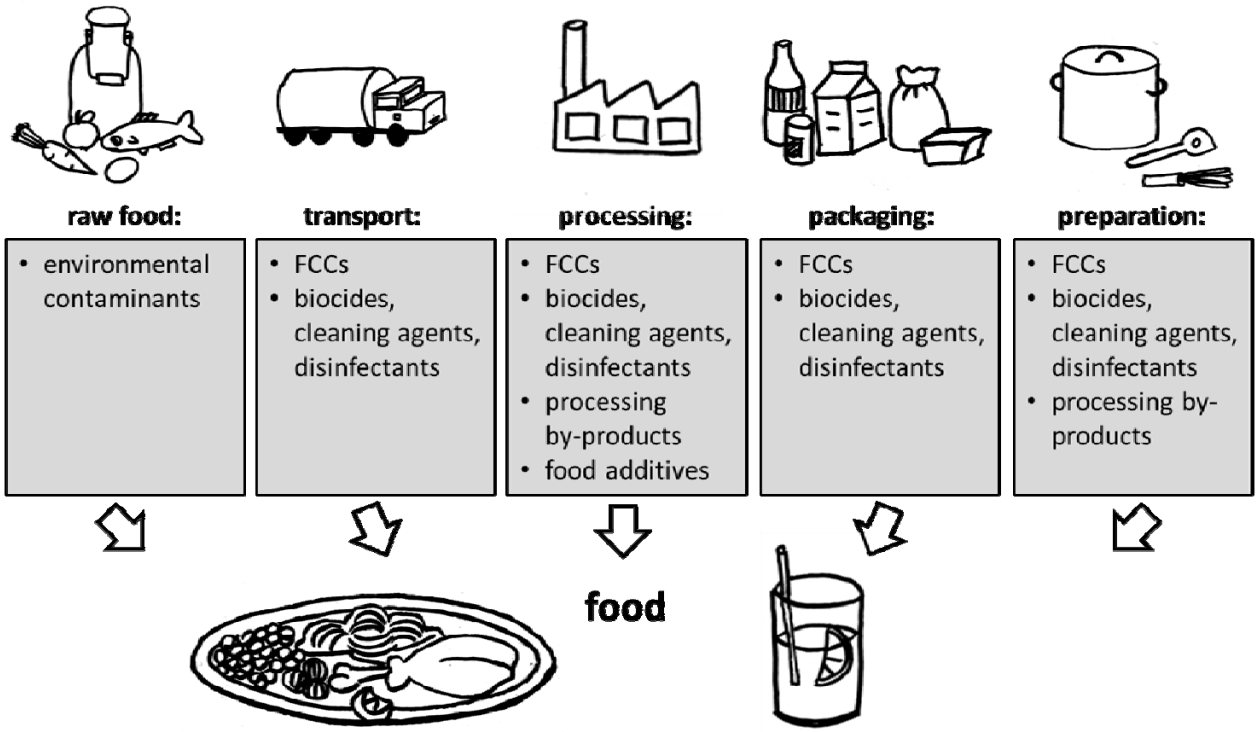

Figure S1. Overview of unintentional chemical inputs into food throughout the food value chain. Chemical contaminants can also be formed in food during (domestic) cooking.

II. Overview of legislation for food contact materials (FCMs) in the US and EU

1. United States

Definitions

The term "food additive" includes substances that are, directly or indirectly, expected to become a component or affect the characteristics of any food under the intended conditions of use (21 U.S.C. §321(s); 21 CFR Part 170.3). "Indirect food additives" (IFA) come into contact with and are transferred into food during e.g. production, processing, packaging, or transport, but they are not intended to be directly added. "Food contact substances" (FCS) are intentionally used as components of any materials coming into contact with food, but they do not have any technical effect in the food (21 CFR Part 170.3(e)). "Food contact articles" are the final products that come into contact with food e.g. food packaging or processing equipment (21 CFR Part 170.3(e)). Safety is defined as "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use" (21 CFR Part 170.3(i)). When determining safety, the probable consumption of a substance, its reaction products in or on food, the cumulative effects of the substance in the diet including any chemically or pharmacologically related substance, and appropriate safety factors shall be considered.

FDA: Food Ingredients and Packaging Terms

Legislation

Any food contact substance that is reasonably expected to migrate into food meets the food additive definition and it will be considered unsafe, unless it is authorized by a Food Additive Petition or acknowledged by an effective Food Contact Substance Notification (FCN). Substances that have been affirmed as Generally Recognized as Safe (GRAS) for use in food packaging, subject to the Threshold of Regulation (ToR), or sanctioned prior to 1958, are exempted from regulation as food additives.

Food Additive Petition: In 1958, the Food Drug & Cosmetic (FD&C) Act of 1938 was amended by section 409 demanding a premarket approval of all new direct and IFAs (21 USC §348). IFAs that have undergone a Food Additive Petition and have been authorized by FDA since then are grouped into (i) adhesives and components of coatings, (ii) paper and paperboard components, (iii) polymers, and (iv) adjuvants, production aids and sanitizers (21 CFR 174-178). Until today, IFAs migrating at levels above 1 mg/kg food require a petition. Toxicological testing guidelines and chemistry recommendations are specified in FDA's Redbook and industry guidance, respectively.

Food Contact Substance Notification (FCN): In 1997, section 409 of the FD&C Act was further amended by introducing the FCN process (21 USC §348(h)). In 2002, the corresponding regulations were completed and codified in 21 CFR 170.100-106. FCNs allow a faster approval of FCS, because FDA is obliged to review the notification, to request further information or respond with an objection or final letter in a defined period of 120 days. FCNs do not undergo a public consultation and are only published after they have been processed by the FDA. FCNs are effective only for the manufacturer and substance covered in the notification. FDA provides guidance for preparing an FCN.

Threshold of Regulation (ToR): Chemicals migrating below 0.5 µg/kg food (corresponding to 1.5 µg/person/day) are exempted from regulation, because exposure is assumed to be negligible (21 CFR

170.39). Their chemical structures shall not contain any groups that may cause genotoxic effects, but toxicological testing is not required.

Generally Recognized as Safe (GRAS; 21 U.S.C. §321(s), 21 CFR 186): Substances that are GRAS under their intended conditions of use are not regulated as food additives and do not require premarket approval by FDA. FCS may be considered GRAS based on scientific data about their use and safety. Establishing GRAS status is based on expert opinion. FDA lists 16 indirect food substances that the agency determined to be GRAS. A non-exhaustive listing of GRAS substances can be found in FDA's database of GRAS notices, at 21 CFR 186 and 21 CRF 182 and 184.

Prior Sanctioned (21 USC. §321(s), 21 CRF 181): Substances that have been used in FCMs before 1958 have not necessarily been risk assessed and it is likely that their safety has been determined based on the experience of use rather than based on scientific data.

Infant food: FCS require specific data (Neal-Kluever et al. 2014).

FDA: Determining the Regulatory Status of Components of a FCM

2. European Union

In the EU, materials and articles intended to come into contact with food are covered by Regulation EC 1935/2004 (Framework Regulation). According to Article 3 of the Framework Regulation no FCMs shall "transfer constituents into food at levels that endanger human health". The Framework Regulation lists seventeen groups of FCMs and food contact articles (FCAs) that may be covered by specific measures. Specific legislations have been adopted for plastics (Regulation EU 10/2011) and recycled plastics (Regulation EC 282/2008), active and intelligent materials and articles (Regulation EC 450/2009), regenerated cellulose film (Directive 2007/42/EC), and ceramics (Directive 84/500/EEC). Further FCM specific measures address epoxy coatings (Regulation 1895/2005/EC) and N-nitrosamines and N-nitrosatable substances (Directive 93/11/EEC).

For all other materials EU-wide, harmonized legislation does currently not exist, but national measures may be in place and the principle of mutual recognition may be applied. The Joint Research Centre provided an overview of the non-harmonized FCM legislation (JRC 2017).

For the manufacture of plastic FCMs, more than 900 starting materials (including monomers) and additives have been authorized. Authorizations have been granted by the European Commission (EC) based on scientific opinions provided by the European Food Safety Authority (EFSA). For substances from the positive list, restrictions may apply and specific migration limits may be set.

EC FCMs: Legislative lists , Database of authorized substances, migration limits and restrictions

III. References and further information

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