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Including non-dietary sources into an exposure assessment of the European Food Safety Authority: The challenge of multi-sector chemicals such as Bisphenol A

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ABSTRACT

In the most recent risk assessment for Bisphenol A for the first time a multi-route aggregate exposure assessment was conducted by the European Food Safety Authority. This assessment includes exposure via dietary sources, and also contributions of the most important non-dietary sources. Both average and high aggregate exposure were calculated by source-to-dose modeling (forward calculation) for different age groups and compared with estimates based on urinary biomonitoring data (backward calculation). The aggregate exposure estimates obtained by forward and backward modeling are in the same order of magnitude, with forward modeling yielding higher estimates associated with larger uncertainty. Yet, only forward modeling can indicate the relative contribution of different sources. Dietary exposure, especially via canned food, appears to be the most important exposure source and, based on the central aggregate exposure estimates, contributes around 90% to internal exposure to total (conjugated plus unconjugated) BPA. Dermal exposure via thermal paper and to a lesser extent via cosmetic products may contribute around 10% for some age groups. The uncertainty around these estimates is considerable, but since after dermal absorption a first-pass metabolism of BPA by conjugation is lacking, dermal sources may be of equal or even higher toxicological relevance than dietary sources.

1. Introduction

Bisphenol A (BPA) is a high-production volume chemical (Merchant Research and Consulting, 2013; PRWeb, 2014) and one of the most discussed chemicals of present times (Beausoleil et al., 2013). Concurrently, it is also one of the most investigated chemicals, because it is used in consumer products while suspected to be an endocrine disruptor according to the definition by WHO (UNEP-WHO, 2013). Bisphenol A is used as a monomer in the manufacture of polycarbonate (PC) plastics and in epoxy-based can coatings. Any residual BPA present in the final material or article has the potential to migrate into food with which it comes into contact (Geens et al.,

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2011). It may also be present in water following migration from PC water kettles (Von Goetz et al., 2010) and in drinking water due to migration from epoxy lining of water supply pipes (WUR, 2001; KEMI , 2013).

Owing to the broad interest in and importance of the chemical, the European Food Safety Authority (EFSA) decided to consider for the first time in a risk assessment not only food and food contact materials, but also non-dietary sources of BPA (EFSA, 2015b) to put the dietary exposures into context. Aggregating dietary and non-dietary sources presents a challenge: For calculating exposure via food, chemical concentrations in foods and food consumption data are available from scientific literature and large databases, but for non-dietary sources, e.g. cosmetic products and thermal paper, far less data are available on consumers' use of these products (Manová et al., 2013).

Therefore, for the non-dietary sources, more extrapolations and assumptions are necessary than for the dietary sources. At the same time, the exposure assessment for dietary and non-dietary sources should be as comparable as possible, to allow the comparison of the respective exposure estimates (e.g. in order to identify the most important sources).

The second challenge is that exposure to non-dietary sources involves not only the oral exposure route (ingestion), but also inhalation and the dermal route. Especially for dermal exposure, the percentage absorption by the skin and following uptake into blood is considerably below the normally assumed worst-case assumption of 100% absorption for ingestion in dietary exposure assessment. Therefore, in order to assess the relative source contributions, the exposure assessment needs to focus on the internal exposure, which is derived by multiplying external exposure estimates with respective absorption fractions.

The absorption fractions used for inhalation and dermal uptake are more uncertain than the standard worst-case assumption for ingestion. Therefore, the internal exposure estimates obtained with the source-to-dose modeling approach (forward-calculated exposure) were cross-checked with urinary biomonitoring data. For this, urinary BPA concentrations were translated into internal exposure to "total BPA" as described by Lakind and Naiman, 2008 (backward-calculated exposure). In the case of BPA, which is conjugated in the liver by glucuronidation and sulfation, "total BPA" stands for the sum of conjugated and unconjugated forms. For further risk assessment these two forms need to be distinguished, since only the unconjugated BPA is toxicologically relevant (EFSA CEF Panel, 2015c). In the present work, however, the exclusive focus is on a plausibility check of the forward-calculated exposure estimates by comparison with backward-calculated estimates from biomonitoring data, so that total BPA is the appropriate quantity.

The work presented here was carried out as part of the most recent EFSA opinion on BPA (EFSA CEF Panel, 2015b; 2015c). This article will not add other data or considerations, but aims to condense and present the methodology and data used to estimate exposure in this very extensive EFSA opinion by focusing on the comparison between source-to-dose exposure modeling and biomonitoring-based exposure modeling. It is laid out how biomonitoring can be used in a regulatory context as a plausibility check for the exposure estimates derived by source-to-dose modeling. The latter are an intrinsic part of chemical risk assessment, because they allow the allocation of source contributions and with that the identification of appropriate risk management measures (Von Goetz et al., 2010). At the same time these exposure assessments, especially in the area of non-dietary sources, suffer from data paucity and therefore require making conservative assumptions, which may result in an unwanted degree of overestimation. Since for BPA a number of non-dietary sources had been included in the exposure assessment, such a plausibility check was considered important.

2. Materials and methods

2.1. Literature search and EFSA's call for data

In order to retrieve data on BPA concentrations in food and food contact materials, as well as migration data from food contact materials, a thorough literature search was conducted by an independent contractor using the search words 'Bisphenol' or 'BPA.' The search was refined by screening title and abstract of each article regarding relevance. Additional literature search was conducted by the experts in EFSA's Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) working group and a call for data was launched by EFSA in July 2012 (EFSA CEF Panel, 2015a; EFSA CEF Panel, 2015b). After the application of general eligibility criteria (such as publication period, geographical origin of the samples, sample type and language), each reference was checked by the working group against agreed quality criteria, which lead to the in- or exclusion of the study. These quality criteria included performance criteria of analytical methods such as the LOD, quality control measures, repeatability and recovery, and further the selectivity of the method as well as measures taken to avoid sample contamination. Further details can be found in EFSA CEF Panel, 2015b.

2.2. Sources of Bisphenol A

BPA was reported to occur in various foods. One yet not fully elucidated source seems to be food of animal origin where levels of BPA were reported that cannot be directly linked to packaging (ANSES, 2013). The food sources were divided into those that are relevant for all consumers on a regular level and those that are relevant only for specific subpopulations such as infants fed with infant formula (EFSA CEF Panel, 2015b).

The non-dietary sources that may lead to exposure of consumers were first assessed qualitatively based on source concentrations and intake frequency (see Table 1). All sources that could contribute considerably to chronic exposure by either having high concentrations and/or regular exposure frequencies were assessed quantitatively in the subsequent step of exposure modeling. In the case that only a specific consumer group would be exposed (i.e. for pacifiers), the calculation was not included into the overall exposure calculation, but listed separately. Sources reported to contain low BPA levels and/or taken in only sporadically were qualified as minor and not included in the quantitative assessment.

2.3. Exposure modeling

Exposure modeling from source to dose (forward calculation) is a method to assess the contribution of a source of a substance (such as BPA) to the exposure of a human individual. If all possible sources are known for one individual and their contribution is aggregated (added up), the aggregate exposure equals the exposure of an individual to a specific substance from multiple sources (Meek et al., 2011; Trudel et al., 2011). Also, the relative contribution of each source can be quantified. Since the exposure assessment conducted by EFSA was aimed at performing risk assessment, all relevant consumer groups should be included, and specifically consumer groups that are most vulnerable to endocrine disrupting substances. Since chronic exposure was the target, daily average exposures were calculated.

Consumers therefore were stratified according to age, following a standard EFSA approach (EFSA, 2011): infants (0–6 months, 6–12