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FIP-EFSA-Q-2015-00293: Comment to the public consultation on „Draft Scientific Opinion on recent developments in the risk assessment of chemicals in food and their potential impact on the safety assessment of substances used in food contact materials“

To Whom It May Concern

We would like to thank EFSA for the opportunity to comment on this draft Scientific Opinion. In our view, this document is of great importance for improving the chemical safety of food contact materials (FCMs) in general. Therefore, it is an excellent opportunity to present to all stakeholders the most current scientific understanding underlying chemical risk assessment for FCMs. We have identified several areas of improvement for which we provide comment. With our input we hope to help improve the document so that it does justice to the importance of sharing the most current scientific understanding with all stakeholders, in the interest of best protecting the general public.

A. General comments

1. Overall relevance of the Scientific Opinion

The draft Scientific Opinion is not intended as guidance document, but will form the scientific basis for such a document. Guidance documents are of very high importance as stakeholders will strictly follow them, also for non-harmonized FCMs. Therefore, we are of the opinion that the underlying Scientific Opinion must be of the highest scientific quality, reflecting current scientific understanding and should meet scientific standards, in terms of referencing evidence and making no unsubstantiated claims. It should also be a reference for stakeholders less familiar with the details of FCM risk assessment, and should therefore be written understandably, explaining current approaches and giving scientific evidence in the form of references and reasoning for (changing) the current approach.

In our view, the draft Scientific Opinion does not sufficiently cover all pertinent issues relating to chemical risk assessment for food contact substances. Neither does it explain the current situation and its shortcomings that warrant changes. Ideally, the Scientific Opinion will explain how the current system does not meet the goal of protecting public health, and then detail systematically what changes need to be made to the overall approach.

2. Introduction

We suggest re-organizing the document to first give an introduction that clearly describes current challenges in chemical risk assessment of FCMs and referencing this according to scientific practice. This introduction should comprise: (i) current regime of chemical risk assessment, with model assumptions used, and with required chemical data (e.g. on migration) and tiered toxicological testing data (ii) further specific measures (Fat Reduction Factor (FRF), functional barrier, Specific Migration Limit (SML), Overall Migration Limit (OML)), and (iii) the

occurrence and assessment of non-intentionally added substances (NIAS). In a next section, proposed changes to the current approach should be explained and scientifically justified (giving references). Finally, a discussion of underlying assumptions and associated uncertainties should be included. Thereby it is of importance to discuss the nature of uncertainties, and if possible, to quantify them.

3. Non-intentionally added substances

NIAS are a central issue for FCM chemical safety. A clear definition of NIAS is missing; it is confusing that the draft Scientific Opinion also contains a chapter on oligomers—does EFSA consider oligomers to be NIAS or not? Further, it should be explained to the reader in detail that NIAS form the largest part of migrate for plastic FCMs (and other FCMs, like coatings, paper and board), and that their identification is not always achievable. The report “An investigation into the reaction and breakdown products from starting substances used to produce food contact plastics (FD 07/01)” by UK Food Standards Agency (Bradley and Coulier, 2007) should be referenced here as a central study investigating NIAS and highlighting that “a larger number of substances remain either unidentified or with ambiguous identification only” (Bradley and Coulier, 2007). Implications for chemical risk assessment should be discussed. Further, other publications have analyzed NIAS, for example formed during irradiation of plastic FCM for food sterilization (Castillo et al., 2013). However, ALL migrating substances need to be assessed for their chemical risk, and the Scientific Opinion needs to explain in detail how this can be achieved, especially if the substances are unknown. One possibility is the use of bioassays for a hazard identification (e.g. nuclear receptor binding or cytotoxicity) of the overall migrate; as this area requires further development this is an opportunity for the EU Commission to invest into targeted R&D.

The aspect of NIAS also highlights that chemical risk assessment of FCMs is best carried out in the finished article (Canellas et al., 2015), and not as presently done, on a substance-by-substance approach for starting substances and additives. Here the Scientific Opinion is missing an important opportunity to discuss this issue and make suggestions how the situation could be improved in the interest of public health. For example, in addition to the current approach using positive lists for plastic FCMs starting substances and additives, lists of authorized finished plastics that have been assessed for their overall migrate, including all migrating NIAS, could be introduced.

Impurities are a sub-class of NIAS, and presently they are already part of the application for starting substances or additives for plastics FCMs, and as such evaluated by EFSA. However, these data are not published, and neither is the purity of the starting substance or additive included in the specifications in EU 10/2011, Annex I (“positive list”). This aspect should be discussed in the Scientific Opinion and EFSA has an opportunity here to explain why this information is not considered for sharing with all stakeholders.

Finally, the draft Scientific Opinion discusses the use of the Threshold of Toxicological Concern (TTC) for assessment of NIAS, even those with partially unknown structures. This is not consistent with the requirements of TTC, where a substance’s full structure must be known. Furthermore, it is not consistent with the risk assessment requirements for other chemicals intentionally used in plastic FCMs, because for these actual toxicological testing data must be submitted. Since there is no logical difference in the chemistry between intentionally and non-intentionally added substances, this distinction cannot be based on scientific principles and is therefore, as such, not warranted scientifically. EFSA needs to explain why it is nevertheless making this distinction in the risk assessment between NIAS and intentionally added substances.

4. Migration testing

Migration testing does not always overestimate migration into foods. Notably, in the case of glass jar closures and long storage time (3 years), plasticizers have been found to migrate above the SML (McCombie et al., 2015, McCombie et al., 2012). Fluorocarbons are another example where migration testing underestimates actual migration into foods (Begley et al., 2005, Begley et al., 2008).

The present Scientific Opinion offers an important opportunity for EFSA to explain the current overall migration limit of 60 mg/kg food, and give scientific evidence justifying this number. In the same sense, the practical threshold of 10 µg/kg (“functional barrier”) should be explained and scientific evidence should be given to justify

this level. In particular, many stakeholders assume that the migration threshold of 10 µg/kg food is linked to toxicological aspects, and that migration below this threshold can be considered toxicologically not relevant. EFSA has an important obligation here to clarify that this is not the case.

Furthermore, an analysis published by our organization in 2014 found that several Substances of Very High Concern (SVHC) under the EU chemical regulation REACH (EC 1907/2006) are authorized for use in FCMs (Geueke et al., 2014). In our view, this is a contradiction because for SVHC there is a societal consensus that these substances are undesirable in any kind of product. We suggest a re-evaluation of the authorized use of SVHC in FCMs and, where appropriate, indicating in EU 10/2011, Annex I that migration of SVHC substances must not occur, i.e. be non-detectable at currently achievable levels of quantification (European Union, 2011).

Finally, the cut-off value of 1000 Da is given for migration testing (molecular size). Although it is common practice in the chemical risk assessment of substances from FCM to use this cut-off value (as stated in the draft Scientific Opinion), no scientific justification with proper references is given for this threshold. We suggest that EFSA takes this opportunity to provide this scientific evidence, or discuss its absence. A suggestion is made to change (increase) this cut-off for fluorocarbons as these have a smaller molecular volume than hydrocarbons, and a molecule's volume is said to be more relevant for intestinal uptake, compared to its weight. However, no actual references are given to substantiate this claim, and this should be amended accordingly.

5. Refined exposure assessment

The draft Scientific Opinion explains how exposure-based risk assessment shall be performed. This marks a paradigm shift from the current approach with a fixed model assumption of 1kg of any food consumed per day. The central problem we see here is that for new substances, exposures can only be estimated for the intended use at the time of application for authorization; based on the exposure estimate, toxicity testing requirements would then be established and a TDI is derived. But the substance, once listed on the positive list (if used in plastics) may then have several other uses, in FCM or other products, because once a chemical appears on the positive list stakeholders may assume that the substance is considered safe by the regulator for FCM use, and other manufacturers may choose to use it with higher preference. In total this may lead to a larger exposure which goes under the radar, and is not toxicologically tested for.

Furthermore, the draft scientific opinion does not show why the comparatively simpler, present approach with its model assumptions does not work well—no evidence is given that it is scientifically not tenable. A detailed critique of the present approach has already been compiled (Norwegian Scientific Committee for Food Safety, 2009). We suggest a systematic re-evaluation of the chemicals on the positive list in terms of their actual exposure vs. the current standard exposure model and vs. the refined exposure models proposed in the draft Scientific Opinion. Based on this analysis a decisions can be made whether the present approach is scientifically robust and sufficiently protects public health or if a refined exposure assessment procedure—as suggested in the draft Scientific Opinion—is required.

Notably, the standard assumption of 6 dm²/kg food surface area to food ratio (used for all foods, except for infants and young children according to EU 10/2011, Art. 17) has been criticized several times and shown to be too low—as discussed in the text (European Union, 2011). A more appropriate, higher value should be discussed as has been suggested (Norwegian Scientific Committee for Food Safety, 2009, Poças et al., 2009), to be protective of children consuming small servings, as the ratio increases with decreasing serving size. In the draft Scientific Opinion several assumptions justifying the value of 6 dm²/kg are made without giving any scientific evidence for them. However, in section 8, the adequacy of 6 dm²/kg is questioned again. Moreover, there is a factual error in the text, stating that the content to contact surface ratio of smaller packages is higher than that of larger packages. This is incorrect and should be clarified: Smaller packages actually have a smaller content to contact surface ratio than larger packages, implying that the standard assumption of 6 dm²/kg food is too low.

Another specific measure for exposure estimation, the Fat Reduction Factor (FRF), is not discussed in the draft Scientific Opinion even though it is included in the Plastics Regulation (EU 10/2011, Annex V, Chapter 4) (European Union, 2011). EFSA is missing an important opportunity here to give scientific evidence justifying the use of the

FRF. Further, it is not clear how under a new, refined exposure-based risk assessment approach the FRF would be used. In fact, it can be assumed that its use will be obsolete under such an approach. This should be discussed in the text.

6. Tiered toxicity testing

In the draft Scientific Opinion, a tiered approach for toxicity testing is described. It is based on the exposure estimate for individual food contact substances. The first tier of 1.5 µg/kg b.w./day is derived from the Threshold of Toxicological Concern (TTC). We consider that this threshold is too arbitrarily chosen and should be justified scientifically. More specifically, the threshold of 1.5 µg/kg b.w./day was derived using data from a carcinogenic potency database which exposed rodents to maximum tolerable doses of chemicals, and then extrapolated to tumor incidence at low-dose exposures (Nordic Council of Ministers, 2005). With our current understanding of non-monotonic dose responses this approach is scientifically questionable (Vandenberg et al., 2012). We recommend systematically evaluating the threshold by using more current data with a broader dose distribution, and also including additional timing of exposure and endpoints like neurotoxicity, immunotoxicity and teratogenicity which may be more sensitive than genotoxicity (Dietert, 2010, Grandjean and Landrigan, 2006).

For the second threshold of 80 µg/kg b.w./day EFSA states that it is “pragmatic” and in line with previous SCF guidelines. Here, EFSA misses a chance to adjust its toxicity testing requirements to current knowledge. Also, if one compares these tiers to the current tiered testing approach, they are 1.8 and 1.6 times higher for a 60 kg person (EFSA, 2008). However, this fact is not justified anywhere in the text. The entire tiered toxicity testing approach section would greatly benefit by including scientific evidence for new toxicological understanding; for example, the lowest tier systematic screening should include tests for potential endocrine disruptors (Gore et al.) e.g. using receptor binding assays, and toxicological testing of the overall migrate (of the finished product). Also, to account for current chronic diseases affecting large parts of the EU population, effects on cardiovascular disease and metabolic disease should at least be acknowledged and if appropriate tests exist, their use should be included. We encourage EFSA to invest more effort into this section of the Scientific Opinion, as it is central to prevention of chronic diseases that are caused by certain chemical exposures, and the protection of public health.

In combination with the proposal for more specific, refined exposure-based risk assessment, the tiered toxicological assessment is of great concern because it leaves the door open for misuse. For example, an applicant may file a new substance for a new application and estimate exposure to be low (below 1.5 µg/kg b.w./day) which would command the lowest tier toxicity testing data to be submitted. Once authorized, the substance may then be used, also by other stakeholders, in many other applications, and actual exposure may increase well above 1.5 µg/kg b.w./day or even 80 µg/kg b.w./day. However, there is no discussion of such cases where actual exposure would warrant additional toxicity testing. This shortcoming needs to be addressed in the Scientific Opinion.

B. Specific Comments

1. Chapter 5, p.7: include scientific references (migration simulation vs migration into food)
2. Chapter 6.2, p.12: provide evidence for assumptions on food consumption (surface to volume ratio)
3. Chapter 9.5, p.18: provide evidence for assumptions (molecular weight vs molecular volume; gastrointestinal uptake linked to molecular size)
4. Chapter 6.3, p.19: Chapter should be 9.7; TTC cannot be used on chemicals with unknown or only partially known chemical structures (toxicological assessment of NIAS)
5. Chapter 8, p.13: The second last sentence is incorrect: smaller packages have a *lower* content to contact surface ratio, not a higher ratio.

Again, we wish to express our gratitude to EFSA for providing the opportunity to comment on this important Scientific Opinion, and hope that our input contributes to improving the document, in the interest of public health.

With our best regards,



Prof. Martin Scheringer, President



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