COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Discussion paper on the approach to the risk assessment on dioxin and draft position paper

Background

1. At the September 2020 meeting, COT reviewed the basis and implications of the new EFSA Tolerable Weekly Intake (TWI) for dioxins (TOX-2020-43) and agreed that there were uncertainties over the derivation of the TWI and possible inconsistencies between the animal and human data. The Committee noted that the published opinion was insufficiently transparent on the rationales for the choices of key studies which made it difficult to evaluate the strength of the evidence. These concerns meant that they were unable to endorse the opinion.

2. The COT recommended that a review of the evidence base and derivation of a health-based guidance value (HBGV) based upon this should be undertaken. However, COT acknowledged that a full systematic review of the dioxins database was neither feasible nor practicable.

3. Following the discussions at the October meeting (TOX-2020-49) Members stressed the need for a clear formulation of the scientific questions, including consideration of all risk management challenges, and agreed it would be useful to form a small subgroup to discuss the requirements/problem formulation in more detail. Annex A provides an overview of the discussion and proposed approach by the subgroup.

4. Members acknowledged that the review of dioxins would be a lengthy undertaking and that it would be appropriate to publish an interim position statement. A draft of the interim position paper is provided in Annex B.

Questions to the Committee

i. Does the Committee agree with the proposed approach in Annex A, especially with regard to the endpoints identified and the literature search to obtain all relevant information to answer the scientific question(s)?

ii. Does the Committee agree with the draft position paper in Annex B?

iii. Does the Committee have any other comments?

Secretariat
November 2020

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Discussion paper on the problem formulation and literature retrieval on dioxin

1. Following discussion of the EFSA opinion on dioxins and the implications for risk management, the COT concluded in September 2020 it was necessary to reconsider the evidence base and set its own tolerable daily intake (TDI).

2. The Secretariat considered both the resource implications, approaches for undertaking the review and the on-going work by the working group on synthesising epidemiological and toxicological evidence (SETE) and proposed an action plan at the COT meeting in October 2020. Members stressed the need for a clear formulation of the scientific questions, including consideration of all risk management challenges, and agreed it would be useful to form a small subgroup to discuss the requirements/problem formulation in more detail.

3. Following these discussions, the Secretariat has drawn up an approach to address the scientific questions and proposed action plan for the literature retrieval and is seeking the Committee's view on this approach.

4. The Secretariat proposes to systematically review epidemiological evidence and toxicological evidence for the critical endpoint identified by EFSA namely effects on the reproductive system, focussing on changes in the male reproductive system parameters. As EFSA's systematic literature review should have identified all the relevant literature, the Secretariat proposes to start the COT's systematic literature review approximately six to nine months prior to the publication of the EFSA opinion. This approach will ensure that any newer literature published since the work taken up by EFSA can be identified.

5. To support the evaluation of epidemiological evidence, the Secretariat furthermore proposes to include a systematic search for any publications on meta-analysis, without any date restrictions.

6. The effects on the reproductive system are considered the most sensitive endpoint, in a very specific population. Therefore, the Secretariat proposes to further perform a narrative review of the literature to confirm that other effects are less sensitive and to identify other endpoint(s) in toxicological (animal) studies which may be more relevant to other subpopulations. This will help inform and identify the potential risk in other population groups for any future risk benefit analyses like the SACN/COT report on oily fish. To start the narrative review, the Secretariat proposes

to look at recent reviews of dioxins by other authorities and/or publications in the literature.

Secretariat

November 2020

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Draft position paper on dioxins

1. The COT reviewed the scientific basis and implications for risk management of the new EFSA tolerable weekly intake (TWI) for dioxins and considered that there were uncertainties over the derivation of the TWI and possible inconsistencies between the animal and human data. Given the implications for risk management, the Committee felt that the rationales for the choices of key studies were not sufficiently clear in the published opinion which made it difficult to evaluate the strength of the evidence. These concerns meant that the COT were unable to endorse the opinion and considered it necessary to reconsider the evidence base and set its own tolerable intake.

2. EFSA established a new TWI of 2 pg/TEQ/kg bw, which is 7-fold lower than the previous tolerable intake, based on data from a Russian Children's study, identifying semen quality, following pre- and postnatal exposure, as the critical effect. The COT noted this study appeared inconsistent with the findings in a second study and considered the Russian study to only provide a weak data set. The studies on experimental animals (rodents) included in the EFSA evaluation confirmed that developmental effects occurred at body burdens similar to the those used as the basis for the previous risk assessment. However, the COT considered there were inconsistencies in the animal data presented in the EFSA opinion to and was unclear, in particular, regarding the rationale for the selection of the study to evaluate the critical body burdens. The COT had raised specific concerns about their reliability in 2001 and later FSA commissioned studies to address these concerns which failed to replicate the specific findings but had other reproductive effects at similar body burdens. Overall, the data presented in EFSA's opinion implied that humans were more sensitive to dioxins than rats. However, this would be inconsistent with the existing body of data on dioxins and knowledge on the relative sensitivity of the human and rat aryl hydrocarbon receptor (AHR). Due to these uncertainties, the COT did not agree with the newly established TWI and the 7-fold reduction in the TWI appeared too conservative on the database overall, the Committee was unable to comment on the dietary exposures and whether they should be compared to the new TWI.

3. On the international level there is currently work planned to review the basis and values of the WHO toxic equivalent factors (TEFs), however, this work may not be available for some time.

4. The Committee acknowledges that this review of dioxins will be an extensive and lengthy undertaking. Given that an immediate reduction in the TDI would take decades to take effect, due to the nature of dioxins especially the long half-life in humans, and as the current TDI was based on the most sensitive endpoint in the animal studies and is intended to protect the most sensitive population group, it will be protective for all population groups.

5. Thus, while the re-assessment of dioxin is a necessary and important piece of work going forward the COT does not consider it necessary in the meantime to alter its current advice on dioxins.

Secretariat

November 2020