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Public consultation on the draft opinion on the evaluation on the risks to animal health related to the presence of hydroxymethylfurfural (HMF) in feed for honey bees

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) has carried out a public consultation to receive input from interested parties on the draft scientific opinion on the evaluation on the risks to animal health related to the presence of hydroxymethylfurfural (HMF) in feed for honey bees. The public consultation was launched on 3 December 2021 and was closed on 10 February 2022. The present report contains the comments received during the public consultation and the responses from the EFSA Panel on Contaminants in the Food Chain (CONTAM) to these comments.

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1. Introduction

In line with EFSA's policy on openness and transparency, and in order for EFSA to receive comments on its work from the scientific community and stakeholders, EFSA engages in public consultations on key issues. Accordingly, the draft Opinion on the opinion on the evaluation on the risks to animal health related to the presence of hydroxymethylfurfural (HMF) in feed for honey bees was released for public consultation from 3 December 2021 to 10 February 2022 by means of an electronic comment submission tool together with explanatory text on the scope of the public consultation on the EFSA website (See Appendix 1).

2. Comments received and responses

Comments were received from two interested parties (Table 1).

Table 1: Overview on stakeholder comments received

Stakeholder	Country
Verein der Zuckerindustrie e.V.	Germany
JKI - Julius Kühn Institut - Federal Research Centre for Cultivated Plants	Germany

The comments received were duly evaluated by the WG on HMF in bee feed and the CONTAM Panel and wherever appropriate taken into account for finalisation of the draft Opinion. Table 2 provides a detailed list with all comments as received from interested parties together with EFSA responses and explanations how the comments were considered for finalisation of the draft Opinion.

Table 2: Stakeholder comments and EFSA responses

Stakeholder	Section	Comment	EFSA response
Verein der Zuckerindustrie e.V.	General Comments	<p>The EFSA-Panel comes to the conclusion, that “<i>it is regarded appropriate to mainly rely on the data from Jashimowicz and El Sherbiny (1975) and Gregorc et al. (2020), considering the lowest BMDL to be 1.16 - 18 µg/bee per day</i>”. The study of Gregorc et al., who elaborated the higher BMDL of 18 µg/bee per day, has not been taken into account within the further considerations. Instead, EFSA solely based the main reference point for bee health at 1.16 µg/bee per day. This approach is not comprehensible. It is true that the HMF concentrations used in Gregorc et al. are about twice those used in Jashimowicz and El Sherbiny, and that the number of bees in the feeding studies is lower. However, these cannot be reasons to completely disregard a study.</p> <p>There are some aspects to be considered regarding the study from 1975:</p> <ul style="list-style-type: none"> • Inverted sugar syrups from the 1970s are not comparable with today's products. In nowadays, the inversion is carried out in a more gentle and controlled manner. 	<p>In section 3.1.6.1 (Derivation of a reference point based on benchmark analyses) the studies relevant for more detailed dose-response analysis are discussed and contrasted. As noted in the last paragraph of this section, it is concluded that based on consideration of the differences between studies, including the quantitative analyses of the dose-response data, the CONTAM Panel did not consider it reasonable to disregard the lower end of the BMDL interval across studies in favour of more recent investigations. However, selecting 1.16 µg/bee per day as the “main Reference Point” did not imply that the possibility for higher values was disregarded, as suggested by this comment. In fact, the quantitative uncertainty analysis (section 3.7.5, Table 9) considers the full BMDL interval across studies, assuming that any value in this range is equally probable. The overall conclusions given in the opinion related to the risk characterization, i.e., the likelihood of exceeding the reference point for different exposure durations (20 days to 180 days), noted in the abstract, summary and conclusion, are based on consideration of the full BMDL interval across the two studies, with <i>no</i> preference for any study.</p> <p>The Jachimowicz and El Sherbiny (J&E) study used mostly „synthetic“ test solutions obtained by mixing different sugars to imitate inverted sugar syrups. These artificial inverted sugars were adjusted to pH 3.9 and spiked with commercial HMF to obtain the feeding solutions. Only one real inverted sugar solution with pH 3.9, in which the HMF content was determined analytically, was included for comparison. It is certainly an advantage, if today's sugar syrups are less acidic. However, the J&R study has clearly shown that it is not the pH of 3.9 but the HMF content that accounts for the toxicity (see response to next bullet point).</p>

Stakeholder	Section	Comment	EFSA response
		<ul style="list-style-type: none"> <li data-bbox="703 284 1456 454">• The pH-value of the feeding solution was adjusted with citric acid. It's well known and also demonstrated by Jashimowicz and El Sherbiny that acids and storage time have a big impact on the formation of HMF. Since the HMF content of the different feeding solutions has not been analytically verified, it can be assumed that the feeding solutions contained higher HMF levels than originally calculated. <li data-bbox="703 826 1456 965">• There is a lack of information on the purity of the used HMF. Research has shown that the purity of HMF available for purchase in 1970s was about 97 – 98 %. Therefore, the kind and level of by-products included in the used HMF preparation is unknown. A negative influence on bee health by possible toxic by-products cannot be excluded. <li data-bbox="703 1161 1456 1332">• The Winkler method used to determine the HMF content in the feed solutions underestimates the real HMF contents. The Winkler photometric method is less selective and susceptible to interferences, so that the use of the current HPLC method would probably have analyzed significantly higher HMF contents in the feed solutions used, from which higher BMDLs would have been derived. 	<p data-bbox="1476 284 2098 742">It is clearly a deficiency of the J&E study that the actual HMF concentration in the feeding solutions (prepared from synthetic inverted sugar by spiking with HMF) were not verified analytically. However, the J&E study shows in Table 1 that the pH-dependent formation of HMF decreases very markedly from pH 2.88 (112 mg HMF in 100 mL solution) to pH 3.30 (6 mg). It can be assumed by extrapolation that HMF formation was negligible at pH 3.9 (pH of the feeding solutions). Consistent with this notion is the finding that the „synthetic“ inverted sugar solution adjusted to pH 3.9 with citric acid was as non-toxic as the non-acidified solution; in contrast, inverted sugar solution with pH 3.9 containing HMF was highly toxic (Fig. 2 of the J&E study). Based on the above we do not think that the feeding solutions contained higher HMF levels than originally calculated.</p> <p data-bbox="1476 810 2098 1061">The CONTAM Panel is not aware of research showing the purity of HMF available for purchase in the 1970s. 97-98% purity is quite high and about the same as today's HMF, leaving little room for impurities. Presumably, the unknown impurities in commercially available HMF are, at least in part, formic acid and levulinic acid, which originate from degradation of HMF (see 1.1.4.2) and which were shown by Bailey (1966) to have about the same toxicity as HMF.</p> <p data-bbox="1476 1173 2098 1401">In general, an analytical method that is less selective and prone to interferences gives higher values than a selective one. Therefore, HPLC analysis should give lower values than the Winkler method. This has indeed been found for HMF in the study by Zappala et al. (2005), as reported in section 1.1.4.4. The Winkler method, the White method, and the HPLC method yielded comparable results in a study by The International Honey Commission (Bogdanof,</p>

Stakeholder	Section	Comment	EFSA response
		<ul style="list-style-type: none"> The age of the bees was not determined <p>For these reasons, the study of Jashimowicz and El Sherbiny should not be given any preference compared to the study of Gregorc et al. Assuming that a worst case consideration led to the solely use of the study from Jashimowicz and El Sherbiny, the mentioned arguments should be taken into consideration.</p> <p>Finally, we would like to point out, that the German <i>Guideline for the Prevention of the Occurrence of Hydroxymethylfurfural in Feed for Honeybees</i>, which is based on scientific studies, is practice oriented and well established in Germany for a couple of years. Link: Merkblatt HMF (bund.de)</p>	<p>2009) and all three analytical methods were recommended for the determination of HMF (see 1.1.4.4.).</p> <p>The age of the bees was 0-3 days, as stated in the J&E study.</p> <p>See first response above.</p> <p>Thank you. The guideline has been considered by the CONTAM Panel.</p>
JKI - Julius Kühn Institut - Federal Research Centre for Cultivated Plants	General comments	<p>Comment of the Lower Saxony State Office for Consumer Protection and Food Safety Institute for Apiculture Celle (Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit Institut für Bienenkunde Celle (LAVES IB CE)) and the Julius Kühn-Institute (JKI). The LAVES IB CE and JKI would like to thank EFSA for the evaluation and for the possibility to submit further information on the state of art-</p> <p>The German authorities BMEL and BVL discussed in the risk assessment of HMF in bee feed in 2015 and thereafter developed a leaflet based on the scientific information available as well on own studies of the LAVES IB CE.</p> <p>In this context the study Lüken, D.J., von der Ohe, W. (2016): Aufklärung der Wirkung des Gehaltes an Hydroxymethylfurfural (HMF) in Futtermitteln für Bienen hinsichtlich der Tiergesundheit und des Carry overs von HMF in Honig. Schlussbericht zum Forschungsauftrag, BLE-Projektträger-Datenbank, Projekt-nummer 314-06.01-2815HS002 was published by the Federal Office for Consumer Protection and Food Safety in Germany. The findings of the study were summarized in the leaflet BVL - Startseite - Merkblatt über die Vermeidung des Vorkommens von Hydroxymethylfurfural in Futtermitteln für Honigbienen (bund.de)</p>	<p>Text on the study has been inserted in various sections and its results have been considered for finalizing the opinion.</p>

Stakeholder	Section	Comment	EFSA response
		<p>The leaflet may be of interest for EFSA, as it covers the topic of HMF. As a general conclusion based on our findings and knowledge, we support the conclusions of the draft scientific opinion of EFSA.</p> <p>We support the recommendations (Chapter 5, p. 68):</p> <ul style="list-style-type: none"> • Further chronic toxicity tests of HMF on honey bees are necessary for the more detailed risk assessment of HMF • For estimating the worst-case scenario of HMF uptake during overwintering it is important to generate more consumption data • A maximum level of HMF for bee feed at the time of delivery should be established • Bee feed should be labelled with use-by date and storage conditions <p>The following documents (Lüken DJ and von der Ohe W, 2016; Lüken DJ and von der Ohe, no date) were uploaded by JKI. The documents and statement were provided by LAVES Bee Institute Celle. The content is fully shared by JKI, and therefore represent our joint view.</p>	<p>Thank you. Note that ML setting and product labelling are not within the remit of EFSA and thus such recommendations cannot be made.</p>

3. References

Lüken DJ and von der Ohe W, 2016. Aufklärung der Wirkung des Gehaltes an Hydroxymethylfurfural (HMF) in Futtermitteln für Bienen hinsichtlich der Tiergesundheit und des Carry overs von HMF in Honig (Evaluation of the effect of the HMF level in bee feed on animal health and on the transfer of HMF in honey). Schlussbericht zum Forschungsauftrag, BLE Projekträger-Datenbank, Projektnummer 314-06.01-2815HS002 (Final report on the research assignment, project sponsor database of the Federal Office for Agriculture and Food, project number 314-06.01-2815HS002). IN GERMAN Available from: https://service.ble.de/ptdb/index2.php?detail_id=57202&site_key=145&zeilenzahl_zaehler=589&NextRow=40&pId=57202&dId=321065

Lüken DJ and von der Ohe W, Darstellung, not dated. Wertung sowie mögliche Umsetzung oder Anwendung der Ergebnisse in Bezug auf den Entscheidungshilfebedarf des. Available from: https://service.ble.de/ptdb/index2.php?detail_id=57202&ssk=9ddea1dad7&site_key=145&stic_hw=hmf&zeilenzahl_zaehler=1#newContent

4. Appendix 1 – Scope of the consultation

EFSA's Panel on Contaminants in the Food Chain (CONTAM) has launched an open consultation on the draft scientific opinion on the risks for animal health related to the presence of hydroxymethylfurfural (HMF) in feed for honey bees. This document presents estimations of exposure to HMF in honey bees via uptake of bee feed and an assessment of health risks for bees related to the exposure to HMF. Interested parties are invited to submit their comments by the indicated deadline. When submitting specific comments to certain lines or paragraphs, reference to the line and page numbers to which the comments relate must be made. Additional data or files to support the comments may be submitted using the relevant function in the digital form. If data on chemical contaminants are submitted to support a comment, these must be submitted in SSD format to the EFSA Data Collection Framework (DCF) via the call for collection of chemical contaminants occurrence data in food and feed. Please contact data.collection@efsa.europa.eu for further information and to receive the access credentials for the DCF web interface. Comments will not be considered if they:

- are submitted in other languages than English;
- are submitted after the closing date of the consultation; • are still in 'draft' status on the closing date of the consultation;
- are presented in any form other than what is provided for in the instructions and the relevant function in the tool (e.g. comments made by email will not be considered);
- are made outside the corresponding fields of the form, for instance as part of supporting files uploaded in the tool;
- are not related to the contents of the document or scope of the consultation;
- contain complaints against institutions, personal accusations, irrelevant or offensive statements or material;
- are related to policy or risk management aspects, which are out of the scope of EFSA's activity. Comments will be assessed in line with the criteria above and taken into consideration if found to be relevant.

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