TECHNICAL REPORT

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Outcome of a public consultation on the draft risk assessment of aflatoxins in food

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) carried out a public consultation to receive input from interested parties on the draft risk assessment of aflatoxins in food. This draft scientific opinion was prepared by the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel), supported by the Working Group on Aflatoxins in food. The draft opinion was endorsed by the CONTAM Panel for public consultation on 25 September 2019. The written public consultation was open from 4 October 2019 until 15 November 2019. EFSA received comments from 14 different interested parties. EFSA and its CONTAM Panel wish to thank all stakeholders for their contributions. The present report contains the comments received and explains the way they have been considered for finalisation of the opinion. The opinion was adopted at the CONTAM Plenary meeting on 30 January 2020 and published in the EFSA Journal.

Key words: aflatoxin, liver, cancer, occurrence, exposure, food, margin of exposure (MOE), public consultation

Requestor: European Commission

Question number: EFSA-Q-2019-00165

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Table of contents

1. Introduction

1.1. Background and Terms of Reference as provided by the requestor of the opinion

1.1.1. Background

In the *Codex Alimentarius* and, more specifically, in the Codex Committee on Contaminants in Food (CCCF), discussions on maximum levels (MLs) and an associated sampling plan for aflatoxins in different foodstuffs are ongoing.

At the 12th session of the CCCF in March 2018 (CCCF, 2018), discussions on MLs for aflatoxin total (AFT) in ready-to-eat peanuts (§103 – §115 of the report) and spices (§116 – §119 of the report) were held but were suspended because of divergent views. The EU could not agree on the discussed MLs for AFT in ready-to-eat peanuts (European Commission, 2018a), taking into account the outcome of the EFSA risk assessment (EFSA CONTAM Panel, 2018), nor could it agree on the MLs discussed for certain spices (European Commission, 2018b). New work was agreed at the 12th session of the CCCF on setting MLs for aflatoxins in cereals and cereal-based food, including food for infants and young children.

In view of the future discussions at the CCCF on MLs for aflatoxins in food and taking into account the recommendations in the last above-mentioned Opinion of EFSA on the effect on public health of a possible increase of the ML for AFT in peanuts (EFSA CONTAM Panel, 2018), it is necessary that EFSA performs a comprehensive risk assessment related to the presence of aflatoxins in food.

1.1.2. Terms of Reference

In accordance with Art. 29 (1) of Regulation (EC) No 178/2002[1], the European Commission asks the European Food Safety Authority for a scientific opinion on the risks to public health related to the presence of aflatoxins in food.

1.2. Rationale for the public consultation and brief summary of its outcome

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 together with its annexes was released for public consultation from 4 October 2019 until 15 November 2019 by means of an electronical comment submission tool together with explanatory text on the EFSA website (See Appendix 1). Comments were received from 14 interested parties from 7 countries. Table 1 provides an overview on the interested parties that have submitted comments through the electronic submission. No comments were submitted by email.

Table 1: Overview on stakeholder comments received

Stakeholder	Category [(a)]	Country
MOLL Marzipan GmbH	Private section (e.g. industry, consultancy, etc)	DE
Federation of European Rice Millers	Private section (e.g. industry, consultancy, etc)	BE
Food Standards Agency	National Authority	UK
Istituto Superiore di Sanità - Unit "Food, Nutrition and Health	University/Public Research Institute	IT
German Federal Institute for Risk Assessment (BfR), EFSA Focal Point	National Authority	DE

[1] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

National Research Council	University/Public Research Institute	IT
European Flour Millers	Private section (e.g. industry, consultancy, etc)	BE
FRUCOM	Private section (e.g. industry, consultancy, etc)	BE
Human Biomonitoring Initiative (HBM4EU Initiative)	University/Public Research Institute	NA
The Wonderful Company	Private section (e.g. industry, consultancy, etc)	USA
Aegean Exporters' Associations	Private section (e.g. industry, consultancy, etc)	Turkey
European Snacks Association	Private section (e.g. industry, consultancy, etc)	BE
European Dairy Association (EDA)	Private section (e.g. industry, consultancy, etc)	BE
National Institute for Public Health and the Environment	University/Public Research Institute	NL

(a): As specified by the commenter.

2. Assessment of comments and use for finalisation of the opinion

The comments received were duly evaluated by the EFSA WG on Aflatoxin in food and wherever appropriate taken into account for finalisation of the draft opinion. Table 2 provides a detailed list with all comments received from interested parties together with EFSA responses and explanations how the comments were considered for finalisation of the draft opinion. Some comments, especially those suggesting editorial changes, have been directly addressed in the text of the opinion, if they were considered appropriate. Identical comments that were submitted by one stakeholder twice or more are included only once in Table 2.

Table 2: Stakeholder comments and EFSA responses

Stakeholder	Comment number	Chapter	Comment	EFSA response
MOLL Marzipan GmbH	1	2.3.2. Data analysis	Topic 1) reliability of used results: You mentioned in your Scientific Opinion, that a careful data analysis has been carried out. Is it mandatory in your procedure, that only data from labs are used, who are able to demonstrate, that their used aflatoxin method meets the |z| score of <=2 and the lab deliver reliable results? Topic 2) origin of used results: Have you differed between data from suspicious samples and from routine samples? Or between raw materials and final consumer products? Have you sorted out data from raw material lots (incoming good control), which have been withdrawn from the market as these did not meet the EU limits (means: consumers were not affected by this not-marketable food)? The more results from suspicious samples or raw materials (before processing) you use, the higher the aflatoxin average will be. This may lead to misinterpretations of aflatoxin real presence in food.	The majority of the occurrence data used for the dietary exposure assessment was collected by competent authorities within the official monitoring programs. It is the responsibility of the Member States and the laboratories to generate data with reliable and validated methods. The majority of these laboratories were accredited and the methods used validated, and for a small part of the samples this information was not provided. Over the time of this opinion, it was not obligatory to report on these parameters. Information regarding participation in proficiency tests (including z-scores) is not requested by EFSA. The following information regarding the sampling strategy is provided in Section 3.2.1. of the Scientific Opinion: *"a part of the analytical results (12%) was obtained by suspect sampling. There were no differences observed between mean concentrations of samples collected via different sampling strategies. Therefore, the CONTAM Panel decided not to exclude any samples on the basis of the sampling strategy."* Insufficient information was available in the EFSA Chemical Occurrence database to separate samples that were not subject to sorting or any other physical treatment from samples that are intended for direct human consumption. Therefore, all available samples were used in the exposure assessment. This may lead to an overestimation of the exposure. The text in

Stakeholder	Comment number	Chapter	Comment	EFSA response
			Topic 3) representative status of used results: how many samples from oilseeds / tree nuts have been used?	the uncertainty section (3.5.2. and Table 21) has been updated to make this clearer. The CONTAM Panel does not agree with the assumption that all samples on the market comply with the ML that is currently in place. In practice, a certain percentage of samples on the market will exceed the ML, and therefore, an underestimation of the risk is made when using the ML as cut-off value for occurrence data. The CONTAM Panel acknowledges that it was not sufficiently clear to the reader which occurrence data were used for exposure assessment. Therefore Table B.8 was added to Annex B.
Federation of European Rice Millers	2	Abstract	The MOE range that is reported in the abstract refers to the imputed exposures from individual country surveys using LB (higher MOE) as well as UB (lower MOE). The analytical data of the foods used and reported in the relevant sections of the opinion were to more than 90 per cent up to 100 per cent left-censored. We propose to differentiate between LB and UB MOE and to include in the abstract UB only, when less than 90 % of the respective food category were left-censored. Rather the 95th percentile LB is a rather conservative scenario taking the huge amount of LCD into account.	Due to the limited word count, it is not possible to report in more detail in the abstract. However, this comment has been clarified in the summary, main body of the text and conclusions.
	3	Summary	lines 118-131: Because of the high rate of LCD and its importance on the risk assessment, it should be clearly communicated which intake is calculated according to LB and which to UB. Upper bound levels should be checked for regulatory compliance for all age groups so that non-compliance or unenforced exceedance of legal limits are excluded from the assessment.	The CONTAM Panel does not agree with the assumption that all samples on the market comply with the ML that is currently in place. In practice, a certain percentage of samples on the market will exceed the ML, and therefore, an underestimation of the risk is made when using the ML as cut-off value for occurrence data. The CONTAM Panel has reported the LB and UB dietary exposure separately in the summary, main body of the text and conclusions.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			For grains and grain-based products, it is unclear which data were available for the assessment, in particular, when it refers to rice. Today, it is not possible to assess whether the data that are available to the industry providing grains for human consumption are in line with those taken into account. This is in particular key for rice, when such samples may be predominantly from targeted sampling at border controls, whereas 60 % of the European rice consumption is of European origin. Similar to milk, the data on 'grains and grain-based products' should be presented in the Opinion down to that level that it is described, i.e. down to rice or corn when both significantly contribute, but other grains like wheat may not.	The CONTAM Panel acknowledges that it was not sufficiently clear to the reader which occurrence data were used for exposure assessment. Therefore, Table B.8 was added to Annex B. The inclusion of a detailed occurrence table on AFB1 and AFT in the main body of the text would result in a large, incomprehensible table and therefore the data are only presented in the Annex. Where it was possible to report this level of detail in the main body of the text, i.e. for AFM1, this was done.
	4	1.3. Supporting information for the assessment	We wonder whether EFSA should recommend that the LOQs should have a sensitivity that enables the testing of compliance with legal limits, i.e. for infant formulae and processed cereal-based products for infant and young children 0.1 µg/kg and for grains and grain-based products (as consumed) a maximum of 0.5-1.0 µg/kg for enabling a better risk assessment. Data from less sensitive methods should not be taken into account for risk assessment. The use of ELISA should be limited to milk only, due to the potential of cross-reactivity in compound matrices with more complex ingredients. The use of ELISA-based methods, in particular kits, requires a thorough validation of each matrix: i.e. an ELISA method that is validated for wheat grains requires an additional validation for wheat gluten or rice kernels.	The CONTAM Panel noted that, for food for infants and small children, some samples were analysed by a method with an LOQ exceeding the ML. These samples were excluded from the dataset as described in Section 3.2.1. A check of the data on grains and grain-based products showed that the highest LOQ reported was 1 µg/kg, which is 2 times lower than the lowest ML. Therefore, no data were excluded based on this criterion. The majority of the occurrence data used for the dietary exposure assessment was collected by competent authorities within the official monitoring programs. It is the responsibility of the Member States and the laboratories to generate data with reliable and validated methods. The majority of these laboratories were accredited and the methods used validated.
	5	2.3.2. Data analysis	We miss any guidance as to the application of the UB method in the risk assessment when the LCD dominate (e.g. when P75 and P95 are in fact mathematically "0". In such a case, the mere procedural treatment of UB may not be justified.	The CONTAM Panel applied the generally accepted substitution method (WHO/IPCS, 2009).

Stakeholder	Comment number	Chapter	Comment	EFSA response
	6	2.6 Exposure assessment	In contrast to other EFSA opinions, the conclusion section and reporting of MOE do typically not refer to the particular country survey. This might be useful information in terms of dietary habits in certain countries and worthwhile mentioning in the main text apart from the Annexes.	CONTAM opinions normally do not report MOE values by survey. The dietary exposure is reported by survey in the Annexes and can be used by the interested party to calculate the MOE for a specific survey. The CONTAM Panel considers that the inclusion of such information (i.e. dietary exposure and MOE values by survey) in the main body of the text is too detailed for individual opinions.
	7	3.2.1 Occurrence data on food as submitted to EFSA	As 'Grains and grain-based products' were identified as a main contributor to dietary exposure, we recommended to have the relevant data published similar to those for milk and dairy products in order to allow the identification of the significant foods on lower FoodEx hierarchy levels. We propose to also include the origin of the foods (EU or non-EU), if this information is available. Lines 2138ff: in line with table 21, it should be mentioned in this section, too, that the official monitoring programmes are risked-based, i.e. they are prone to overestimates. Re. Table 8, Table 12 and Annex B.5 to B.7: We wonder about the justification of applying the UB calculation for a risk assessment, when more	The CONTAM Panel acknowledges that it was not sufficiently clear to the reader which occurrence data were used for exposure assessment. Therefore, Table B.8 was added to Annex B. The inclusion of a detailed occurrence table on AFB1 and AFT in the main body of the text would result in a large, incomprehensible table and therefore the data are only presented in the Annex. Where it was possible to report this level of detail in the main body of the text, i.e. for AFM1, this was done. The CONTAM Panel usually does not include information regarding the origin of the foods as once these foods are available on the EU market, the origin is no longer considered. Section 3.5.2. includes the following sentence: "*The available occurrence data have been in part collected via a risk-based monitoring strategy and this may overestimate the background aflatoxin levels*". The CONTAM Panel considers that it is sufficiently clear and does not see the need to repeat this in Section 3.2.1. As specified in Section 2.6: The food categories represented by either a very low

Stakeholder	Comment number	Chapter	Comment	EFSA response
			than 90 % of data are left-censored: For example, in no sample of 'alcoholic beverages' aflatoxins were measured. Nevertheless, the UB was set at 1 µg/kg. The UB for foods for infants and young children was set at 1 µg/kg. However, the ML is 0.1 µg/kg for such foods, i.e. the risk assessment is based on foods that cannot legally be placed on the market. The same applies to milk: the ML is 0.5 µg/kg. The imputed UB should not be higher for foods to which this ML is applicable. For 'grains for human consumption' we propose to open the data for level 3 (Annex B.7) - which are currently frozen for Aflatoxin M1. The comments above apply proportionately to the data for AFT as well.	number of samples (< 6 samples) or for which all data were below the LOD or LOQ were considered not suitable and were not used for the exposure calculation. The CONTAM Panel acknowledges that it was not sufficiently clear to the reader which occurrence data were used for exposure assessment. Therefore, Table B.8 was added to Annex B. The CONTAM Panel noted that, for food for infants and small children, some samples were analysed by a method with an LOQ exceeding the ML. These samples were excluded from the dataset. A check of the data on milk showed that the highest LOQ reported was 0.05 ug/kg, which is equal to the ML. Therefore, no data were excluded based on this criterion. A filter was applied in Table B.7, due to which the data for the other aflatoxins were not shown. This has been corrected in the final version.
	8	3.2.2 Levels of biomarkers of exposure in the European population	The chapter refers to a publication by Bogalho et al., 2018, who have analysed the occurrence of AFM1 in breast milk and who included a semi-quantitative food questionnaire (7-day recall) on 11 food groups. The results of the dietary intake assessment are not published. Details are not given (confounders, no separate data on corn, no intake data on nuts, legumes, oilseeds or fruit that have been identified as a contributor in the current survey). Therefore, a causal relationship as to the association of rice intake with measured AFM1 levels in breast milk is not established in terms of epidemiological quality criteria. The wording by EFSA should take this into account, e.g. "the authors suggest" is appropriate rather than "it has been shown".	The CONTAM Panel acknowledges the limitations of the study and deleted the sentence from the opinion.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	9	3.3.1 Current dietary exposure assessment	We propose to reconsider whether the UB calculations are appropriate to include in the summary table in the main part of the Opinion, when they are driven by data with more than 90% LCD with/without exceeding legal limits. It should be considered, whether rather the 95th LB maximum is an appropriate worst chronic dietary exposure estimate for risk assessment. It might be helpful to include the countries of the remaining surveys in this table in the main text to visualize the interpretation. Line 2413 makes reference to rice, bread and rolls and fine bakery wares as the main contributors among the subcategories. This sentence is not backed up by the provided data: data on rice are not specifically presented; bread and rolls had 98% LCD, i.e. their contribution can only rely on 10 samples out of 463 with quantifiable levels; in view of fine bakery ware, it raises the question of the contribution of ingredients other than cereals (fats and oils? nuts?).	The difference between LB and UB shows the uncertainty due to the left-censored data. Both LB and UB are presented in an equal and objective way in the opinion. However, to improve clarity the CONTAM Panel has reported the LB and UB dietary exposure separately in the summary, main body of the text and conclusions. The same was done for MOE values calculated based on LB and UB exposures. Data by country are shown in the annexes; inclusion of this information in the main body of the text is considered too detailed and will results in large tables that are difficult to interpret. The CONTAM Panel acknowledges that it was not sufficiently clear to the reader which occurrence data were used for exposure assessment. Therefore, Table B.8 was added to Annex B. Bread and rolls are one of the main contributors, but this is driven by high consumption. The Scientific opinion (Section 3.3.1.2.) has been revised to include this information. The CONTAM Panel noted that most of the quantified results for fine bakery wares contained nut filling. This information was also added to the same section in the opinion.
	10	3.4.1 Risk characterisation based on animal data	For the reasons outlined under comments re 3.3.1, we propose to focus the MOE calculations in the main text on LB calculation and to mention the country surveys in the main text.	The difference between LB and UB shows the uncertainty due to the left-censored data. Both LB and UB are presented in an equal and objective way in the opinion. However to improve clarity, the CONTAM Panel has reported the LB and UB dietary exposure separately in the summary, main

Stakeholder	Comment number	Chapter	Comment	EFSA response
				body of the text and conclusions. The same was done for MOE values calculated based on LB and UB exposures. Data by country are shown in the annexes; inclusion of this information in the main body of the text is considered too detailed and will results in large tables that are difficult to interpret.
	11	3.4.2 Risk characterisation based on human data	For the reasons outlined under comments re 3.3.1, we propose to focus the potency estimates in the main text on LB calculation and to mention the country surveys in the main text.	The difference between LB and UB shows the uncertainty due to the left-censored data. Both LB and UB are presented in an equal and objective way in the opinion. However to improve clarity, the CONTAM Panel has reported the LB and UB dietary exposure separately in the summary, main body of the text and conclusions. From Tables 19 and 20 it is clear which cancer risk estimates relate to LB dietary exposure and which to UB and no further change was done in Section 3.4.2. Data by country are shown in the annexes; inclusion of this information in the main body of the text is considered too detailed and will results in large tables that are difficult to interpret.
	12	3.5.5 Summary of uncertainties	For the huge amount of LCD, an uncertainty towards risk underestimate is mentioned. However, this may play a role for the LB estimates only. As in the current text (in particular in summary, abstract), no clear distinction is made between UB and LB, the reader assumes a much higher risk, whereas the outcome is driven to a large extent due to analytical weaknesses and targeted sampling.	Table 21 gives a summary of the uncertainties which are explained in the text above. It is explained in section 3.5.2. that "*the large proportion of analytical results with left-censored data (values below LOD/LOQ) introduced considerable uncertainties to the exposure estimates. The use of the LB in this Opinion tends to underestimate, while UB tends to overestimate the dietary exposure*." Therefore, no change of Table 21 is needed.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			In terms of the Yeh et al. study, it appears rather questionable that the main confounders like HCV and alcohol consumption have not been taken into account. Furthermore, the study has been conducted in China in the 1980ies where and when many more confounders may have played a role. This all in all is a weakness of the study and it is questionable whether it can nevertheless serve as pivotal study for the European population in 2019.	The CONTAM Panel is aware of the limitations of this study as specified in Section 3.5.4. Despite the fact that new epidemiological studies have been conducted, information is missing to use these new studies in the risk assessment. Recommendations have been formulated to generate new data that would allow to convert biomarker levels into external doses.
	13	5. Recommendations	For a more realistic risk assessment, systematic data with sufficient sensitive method including FoodEx level 3 and level 4 are needed. Without these, risk management measures would largely rely on LCD driven by high-intakes food categories rather than on tangible risks.	The CONTAM Panel would welcome the availability of occurrence data generated with more sensitive methods. Dietary exposure was calculated up to Foodex level 3. Details on the data used for exposure assessment are shown in Annex B, Table B.8.
Food Standards Agency (UK)	14	General	The Opinion on the risk to public health related to the presence of aflatoxins has been referred to the UK's Committee on Toxicity (COT) by the Food Standards Agency (FSA). The FSA has sought the views of our independent Scientific Advisory Committee on the approach used for the risk assessment. As a general comment the Committee noted that the opinion provided a good review of the area and had no major reservations of the risk characterisation.	Thank you
	15	3.1.2 Toxicity in experimental animals	In vitro genotoxicity (lines 1039-1049): The Committee noted that estimating potency using HepG2 cells for compounds that depend on P450-dependent metabolism for their activity is highly questionable as these are not liver cells, they are liver-derived.	This study *in vitro* looked not only at HepG2 cells but used two other cell lines and studied the relative potency based on all three cell lines. The CONTAM Panel noted the limitations of this study and did not use the outcome in the risk assessment. The text in Section 3.1.2.3. was modified to improve clarity.
	16	3.1.4 Mode of action	The Committee noted that there is no discussion on the possible role of liver toxicity as a co-factor in the MoA for AFB1-induced liver cancer. While there is little doubt that AFB1 is a genotoxic hepatocarcinogen, there is ample	The CONTAM Panel added the following text as an introduction to Section 3.1.4.6 in the opinion: "This section focuses on factors influencing susceptibility of humans. The

Stakeholder	Comment number	Chapter	Comment	EFSA response
			evidence that factors that stimulate hepatic proliferation, such as cytotoxicity or viral infection, exacerbate the incidence of tumours.	CONTAM Panel notes that in animal studies at high doses, substances that causes regenerative hyperplasia may exacerbate the incidence of tumours". Additional factors contributing to the susceptibility were already included in Section 3.1.4.6.1.
	17	4.0. Conclusions (overall chapter)	Risk characterisation (lines 2860-2878): The Committee noted that many of the occurrence data (~ 90%) were left-censored, as if often the case with such assessment. Accepting that EFSA took good account of this in their exposure assessment, it does lead to a significant risk communication problem: most exposure scenarios suggest potential concern (in fact it is stated that "The calculated MOEs are below 10,000, which raises a health concern"), yet in many samples levels are not detectable. Hence, either the analytical method needs to be improved or probabilistic risk assessment is needed.	The CONTAM Panel acknowledges that the uncertainty due to the left-censored data is high. However, for AFB1, all MOEs, including MOEs calculated on the LB dietary exposure, were below 10 000. For AFM1, the MOEs calculated from UB data and LB data were below 10 000 for some surveys particularly for the younger age classes. Therefore, the application of a probabilistic risk assessment is not warranted. The CONTAM Panel supports the need for using sensitive methods for the collection of occurrence data as specified in the recommendations.
Istituto Superiore di Sanità - Unit "Food, Nutrition and Health"	18	3.1.1 Toxicokinetics	3.1.1.1.4 Excretion lines 855-856 in principle, AFM1 is excreted to a significant extent also in other dairy ruminants farmed in the EU: sheep, goat, water buffalo see eg, (Rahimi E, Bonyadian M, Rafei M, Kazemeini HR. Occurrence of aflatoxin M1 in raw milk of five dairy species in Ahvaz, Iran. Food Chem Toxicol (2010) 48(1):129–31). However little data exist to quantify the excretion rate	Thank you for sharing this reference with the CONTAM Panel . Considering the large differences in concentrations among geographic regions, the CONTAM Panel took only occurrence data sampled in the EU into account. Data on the occurrence in milk from animal species other than bovine were included in the assessment as explained in the reply to comment number 20.
	19	3.1.6 Possibilities for derivation of a health-based guidance value (HBGV)	According to the evidence provided in the draft opinion, AFG2 is not genotoxic *in vitro* (lines 85-86 and 1139-1149), does not cause DNA damage (line 352) and cannot form the 8,9-epoxide (line 877); thus the evidence for genotoxicity appears to derive from its belonging to the aflatoxin group. The "inadequate evidence" for carcinogenicity evaluated by IARC (2012) simply means lack of robust data; moreover no new *in vivo* data are available (line 2104). Conversely, it cannot be excluded that AFG2 may exert hepatotoxicity and promote liver tumours also through non-genotoxic mechanisms.	The CONTAM Panel included the following sentence in Section 3.1.6.: "*The CONTAM Panel considers that this conservative approach is appropriate in this case, but notes the uncertainty arising from the insufficient data available on AFB2 and AFG2.*"

Stakeholder	Comment number	Chapter	Comment	EFSA response
			Therefore, it is correct that AFG2 is considered in the risk assessment; however it should be made clear that to group AFG2 together with AFB1 is a conservative assumption to take into account the insufficient data on toxicology, and in particular carcinogenicity. Much the same considerations do apply to AFB2. Indeed, based on available scientific data, it does not make much sense to attribute a potency factor of 0.1 for the genotoxic AFM1 and to consider AFG2 and AFB2 as of equivalent potency compared to AFB1 Accordingly, lines 2103-5 should be modified as follows "Therefore, in the absence of new in vivo data to quantify differences between the individual aflatoxins, the CONTAM Panel applied equal potency factors for AFB1, AFB2, AFG1 and AFG2 as used in previous assessments. The Contam Panel considers that this conservative approach is appropriate in order to take into account the important uncertainty deriving from the overall insufficient data on AFB2 and AFG2".	
	20	3.2 Occurrence data	Line 2264 Occurrence data on AFM1 Other ruminant species, namely sheep, goat and water buffalo, produce dairy products that have a significant role in the EU diet, with remarkable differences among Member States (see the data on sheep population distribution in the EU, EFSA AHAW 2014). However, there are no data to assess the contribution to AFM1 exposure by the consumption of milk and dairy products from these species	Occurrence data on milk from cows, sheep, buffalos, goats and donkeys were available (Annex B, Table B.7) and were used for the exposure assessment. However, considering the similar mean concentrations and the low number of samples for some milk types, these milk samples were grouped.
	21	3.2.3 Processing	Cheese-making is a relevant processing procedure for AFM1, because of the binding with the protein fraction of milk, and in particular the preferential binding to casein during milk coagulation (Bognanno M, La Fauci L, Ritieni A, Tafuri A, De Lorenzo A, Micari P, et al. Survey of the occurrence of Aflatoxin M1 in ovine milk by HPLC and its confirmation by MS. Mol Nutr Food Res (2006) 50(3):300–5). Therefore, AFM1 is liable to concentrate in cheese, preferentially with high protein content (like Parmigiano, see lines 2267-68). The Italian National Food Safety Committee in 2013, based on available data and calling for more information on specific cheese types, established the	Thank you for sharing this information with EFSA, which is in line with the observation of high mean concentrations of AFM1 in cheese (Table 12). The CONTAM Panel did not calculate AFM1 concentrations in cheese based on processing factors but used instead the concentrations measured in cheese samples.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			following concentration factors: 3.0 for soft cheeses (e.g., mozzarella) or whey-derived products (e.g., ricotta), 5.5 for hard cheeses (e.g., parmigiano). Based on these factors, 1 ng Aflatoxin M1 per kg whole milk will become 3 ng/kg or 5.5 ng/kg in a soft or hard cheese, respectively (opinion available in Italian at http://www.salute.gov.it/imgs/C_17_pubblicazioni_2017_allegato.pdf)	
	22	5. Recommendations	- line 2880. The recommendation should be more general "Data are needed to clarify the genotoxic and carcinogenic potentials of AFB2 and AFG2." - lines 2885-86: AFM2 cannot currently be included into risk assessment because of lack of data on both occurrence and toxicology. Thus the recommendation should be amended as follows: "More data are needed regarding the occurrence of aflatoxicol as well as the occurrence and toxicology of AFM2, to clarify whether these substances should be included in the risk assessment" - furthermore, the following additional recommendation is indicated: "Data to refine the exposure assessment of AFM: contribution of milk and dairy products from ruminant species other than cattle; transformation factors to assess the transfer from milk to dairy products."	The wording of the recommendation was revised as suggested. The wording of the recommendation was revised. The CONTAM Panel considers that understanding the occurrence of AFM2 and aflatoxicol in food is the first step. At the level of the EU, the contributions of milk and dairy products from other animal species than cows are limited and therefore such a recommendation at EU level is not considered appropriate. The CONTAM Panel prefers to use concentrations measured in the products as consumed instead of using transformation factors.
German Federal Institute for Risk Assessment (BfR)	23	1.3. Supporting information for the assessment	Line 276 - 279, p. 9 Comment: The opinion is focused on aflatoxins in food with regard to human health. For the food category milk and milk products the AFM1 contents resulted by the intake of contaminated feed via the animals. However, this context is mentioned in the current opinion marginally. Remark: The possible transfer of aflatoxins from feed into food such as milk is focused	Thank you for this comment. The CONTAM Panel took the available occurrence data on food of animal origin into account in the dietary exposure assessment. However, the transfer of aflatoxins from feed to food of animal origin was not included in the scope of this opinion. A sentence has been added to Section 1.2 to make this clear to the reader.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			in a previous EFSA report (EFSA 2004). However, it should be evaluated if this report needs a revision.	
	24	3.1.1 Toxicokinetics	Chapter 3.1.1.1.4 Excretion, Line 825 - 826, p. 26 Comment: What is with a possible transfer of AFB1 from feed into other food of animal origin than milk (e.g. egg, meat)? Remark: Is there a significant impact of AFB1 for humans via other food of animal origin?	The transfer of aflatoxins from feed to food of animal origin was not included in the scope of this opinion. A sentence has been added to Section 1.2 to make this clear to the reader. The CONTAM Panel noted that there is potential for transfer of AFB1 into food of animal origin but this is only relevant at high feed concentrations which are not likely to occur given the EU legislation.
	25	3.2.1 Occurrence data on food as submitted to EFSA	Chapter 3.2.1.2 Occurrence data considered for dietary exposure assessment, Line 2280 - 2286, p. 72 Comment: What could be a reason for a difference between conventional and organic farms? Or are the AFM1 concentrations in milk from organic farms in general lower than in conventional farms? The analytical results are not mentioned in the text as well as in Table 12 or in Annex D, Table D.2. Remark: A differentiation between different production systems without regarding the fed feed materials should not be a part of the present opinion.	The data are included for information in Annex D Table D.2. Due to the limited number of samples and high percentage of left-censored data no conclusions can be drawn. Considering that the opinion relates to food, there is relevance to this information.
	26	3.4.2 Risk characterisation based on human data	Line 2628 ff, p. 84 Comment: The implementation of a model calculation (either within the opinion itself or in the appendix) would improve the comprehensibility of the cancer risk estimates. Otherwise, a cross reference to page 171 of the FAO/WHO publication from 2018 where the calculation is described in more detail could be included. FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2018. Aflatoxins (addendum). Evaluation of certain	The CONTAM Panel included the information in Section 3.4.2.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			contaminants in food (Eighty- third report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). 3-280.	
	27	5. Recommendations	Line 2885/2886, p. 92 Comment: In the introduction, it is stated that the fungi also form other mycotoxins, e.g. sterigmatocystin (STC), which is a precursor of aflatoxin B1 and G1. As STC is also a genotoxic carcinogen causing among others hepatocellular carcinomas (HCC) it should be suggested to recommend also the generation of more data on the co-occurrence of aflatoxins and STC to clarify whether STC should be included in the risk assessment.	In 2013, the CONTAM Panel concluded: "*Sterigmatocystin (STC) shares its biosynthetic pathway with aflatoxins. A. nidulans and A. versicolor are apparently unable to biotransform STC into O-methylsterigmatocystin, the direct precursor of aflatoxin B1 (AFB1) and G1 (AFG1). Consequently, substrates colonised by these fungi can contain high amounts of STC, while substrates invaded by A. flavus and A. parasiticus contain only low amounts of STC as most is converted into AFs.*" Nevertheless co-exposure may occur via different foods consumed at the same time or colonisation of a crop by different fungal species. Therefore, the assessment of STC and aflatoxins in a mixture approach is appropriate. However, in the current assessment the CONTAM Panel prefers to focus in its recommendations on the generation of data that would allow to reduce the uncertainties.
National Research Council	28	Summary	There is a direct relationship between the environmental conditions of temperature and humidity and a greater predisposition to the development of mycotoxins depending on the geographical location of the country being considered. It is also important to remember that the survival of aflatoxin-producing microorganisms can also occur in conditions that do not allow it to grow. Moreover, the tolerance towards a given parameter (pH, humidity, temperature, oxygen) increases if the remaining growth conditions return to the optimal range for that particular species, while a combination of sub-optimal factors can prevent fungal growth. From this, it appears necessary to have greater control upstream with tighter rules and tighter controls that tend to reduce the possibility of producing the contaminant in the food and in derivatives such as milk.	The CONTAM Panel acknowledges this comment. Please note that official controls and the implementation of legislation is part of the risk management. EFSA is responsible for risk assessment.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	29	5. Recommendations	In the case of contamination of the food ration administered to animals in livestock production, which goes, consequently to contaminate the milk that arrives on the tables of the final consumer, the controls on the content of AFM1 should be increased, that if it should exceed the threshold values, they are an index of contamination of the administered ration. This would allow backward control of food and its producers.	The CONTAM Panel acknowledges this comment. Please note that official controls and the implementation of legislation is part of the risk management. EFSA is responsible for risk assessment.
EUROPEAN FLOUR MILLERS	30	Summary	For grains and grain-based products, it is unclear which data were available for the assessment, in particular, when it refers to wheat. Today, it is not possible to assess whether the data that are available are in line with those taken into account. Similar to the case of milk and dairy products, the data on 'grains and grain-based products' should be presented in the opinion down to that level that it is described, i.e. down to rice or maize when both significantly contribute. But we believe that it is highly unlikely that grains like wheat may.	The CONTAM Panel acknowledges that it was not sufficiently clear to the reader which occurrence data were used for exposure assessment. Therefore, Table B.8 was added to Annex B. The inclusion of a detailed occurrence table on AFB1 and AFT in the main body of the text would result in a large incomprehensible table and therefore the data are only presented in the Annex. Where it was possible to report this level of detail in the main body of the text, i.e. for AFM1, this was done.
	31	3.2.1 Occurrence data on food as submitted to EFSA	As 'Grains and grain-based products' were identified as a main contributor to dietary exposure, we recommend to have the relevant data published similar to those for milk and dairy products in order to allow the identification of the significant foods.	See previous comment
	32	3.3.1 Current dietary exposure assessment	Line 2413 makes reference to bread and rolls and fine bakery wares as the main contributors among the subcategories. This sentence is not backed up by the provided data: data on wheat are not specifically presented here. Bread and rolls had 98% LCD, i.e. their contribution can only rely on 10 samples out of 463 with quantifiable levels; in view of fine bakery ware, it raises the question of the contribution of the grain or cereal (most probably maize rather than wheat?) but also ingredients other than cereals (fats and oils? nuts?).	The CONTAM Panel acknowledges the comment. Tables E.5 bis (A) and E.7 bis (A) have been added to Annex E and present the contributing foods at the FoodEx level used for dietary exposure for AFB1 and AFT+M1 Bread and rolls are one of the main contributors, but this is driven by high consumption. The Scientific opinion (Section 3.3.1.2.) has been revised to include this information. The CONTAM Panel noted that most of the quantified results for fine bakery wares contained nut filling. This information

Stakeholder	Comment number	Chapter	Comment	EFSA response
				was also added to the same section in the opinion.
FRUCOM	33	General comment	FRUCOM is the European association representing traders in dried fruits, edible nuts, processed fruits & vegetables, and processed fishery products.	
	34	3.2.1 Occurrence data on food as submitted to EFSA	Occurrence data FRUCOM comment: Despite much higher consumption of other food categories, such as grains and grain-based products, there is three times more data in the category legumes, nuts and oilseeds for AFB1 and five times more for aflatoxin total. Table 9 Summary of the AFB1 occurrence data by food category includes 27 772 results for legumes, nuts and oilseeds as compared to 8 979 results for grains and grain-based products. Table 10 Summary of the AFT occurrence data by food category contains 24 507 results for legumes, nuts and oilseeds and 4 860 results for grains and grain-based products. The EFSA opinion does not sufficiently address the fact that nuts and oilseeds are controlled disproportionately which distorts consumption (exposure) estimates.	The CONTAM Panel acknowledges that the number of samples for food categories is different. A low number of samples for a food group is unwanted because it may be unclear whether the data are representative of the food available on the EU market. However, a large number of samples strengthens the dietary exposure assessment.
	35	3.3.1 Current dietary exposure assessment	Exposure FRUCOM comment: we acknowledge the findings below by both JECFA and EFSA and would recommend the EU institutions take them into account: Lines 2409-2413: Contribution of individual food categories to the LB mean chronic dietary exposure to AFB1. The food category 'grains and grain-based products' was the most important contributor to the overall LB mean chronic dietary exposure to AFB1 across all age groups. The LB median contribution among surveys ranges from 38% for adults to 50% for the very elderly, with contributions reaching up to 67% in certain surveys. Lines 2445-2446: Overall, the main contributor to the LB mean chronic dietary exposure to AFT+AFM1 was the food category 'grains and grain-based products' (contributing up to 59% in adolescents). Lines 2510-2520: In 2016, the JECFA calculated international estimates of chronic dietary exposure using the food consumption data from the GEMS/Food cluster diets and a standard body weight of 60 kg (FAO/WHO, 2018). The calculations covered the exposure from cereals, nuts, spices, and other foods such as figs and soy. The mean UB dietary AFT exposure ranged	The CONTAM Panel acknowledges this comment.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			from 1.3 ng/kg bw per day (cluster G08, comprising Austria, Germany, Poland and Spain) to 34.8 ng/kg bw per day (cluster G13, comprising African countries and Haiti). The JECFA reported that a similar pattern of exposure was observed under the LB scenario. The dietary exposure for a high consumer was considered to be twice the mean dietary exposure. Wheat was the main contributor to the UB dietary AFT exposure (range 37–76.5%) for several countries, including many European countries. However, for cluster G10 (comprising European countries such as Italy, Bulgaria, Estonia, Latvia and Lithuania), rice was the main contributor to the UB dietary AFT exposure (range 34.5–80.3%). Lines 2417-2418: Despite relatively high AFB1 concentrations measured in almonds, pistachios and other seeds, the exposure to AFB1 from these foods was small, which is explained by low consumption.	
	36	3.3.1 Current dietary exposure assessment	Contribution of individual food categories Lines 2428-2430: Among the food subcategories, dried fruits (mainly dried figs) contributed up to 48% and dietary supplements up to 27% to the overall AFB1 LB mean exposure. FRUCOM comment: These data stem from contribution of data by a Member State where one particular product is used, and the import statistics of dried figs together with average consumption data demonstrate that these cannot be extrapolated to the EU total. In the final ESFA opinion it should clearly be mentioned that this concerns only one specific Member State and not to apply it on the whole EU market. With regards to Turkish figs we would like to emphasise the controls which are already in place for aflatoxin in figs. The figs are inspected in the dark rooms for fluorescence and any figs which are used for paste, or cut and diced are examined internally as well. Research is being carried out and investment is been made in developing laser devices which have the capability of detecting fluorescence which may be linked to aflatoxin presence, although the industrial application is still limited at present in Turkey. Samples are collected through the production run and tested by the processor for aflatoxin. On completion of a batch, sampling and analysis is carried out	The following text is included in Section 3.5.2. Exposure scenario/exposure model: "*The exposure assessment was based on aflatoxin occurrence data collected in numerous EU countries; however, most of them (~ 65%) were collected in only three Member States while some other countries submitted only a limited number of data. Most of the imported foods, such as nuts and fruits, were sampled in harbour areas and afterwards transported throughout Europe, therefore it is believed that the data for these foods properly covers the EU market. This seems not to be the case for the other food categories largely contributing to the exposure to aflatoxins, in particular 'grains and grain-based products' and 'milk and milk products'. For these food categories, there is uncertainty around possible regional differences in aflatoxin contamination and the data set is likely not to be fully representative of food for the EU market*. "The CONTAM Panel considers that this is sufficiently addressed in the opinion.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			by the Turkish Ministry and the results accompany shipments. Many importers carry out additional sampling which may be independent of processor or exporter. In addition, 20% of containers of Turkish figs are stopped and analysed by the EU Port Health Authorities.	
	37	3.3.3 Previously reported dietary exposure	Maximum levels Lines 2527-2529: Both EFSA and the JECFA performed impact assessments of the implementation of different MLs for specific food commodities on the dietary exposure. Such assessments are outside the scope of the current Scientific Opinion and are therefore not reported in detail. We would like to recall the position of JECFA in 2017 and 2007: • Enforcing an ML of 15, 10, 8 or 4 µg/kg would have little further impact on the overall dietary exposure to AFT in all five of the highest exposed population groups, compared with setting an ML of 20 µg/kg for almonds, Brazil nuts, hazelnuts, pistachios. • Whatever the hypothetical ML scenario applied (no ML, 4, 8, 10, 15 or 20 µg/kg) to dried figs, there would be no impact on the overall dietary exposure to AFT (below 0.03%, equivalent to a dietary exposure of <0.01 ng/kg bw per day). • In 2017 JECFA concluded that enforcing an ML of 10, 8 or 4 µg/kg for ready-to-eat peanuts would have little further impact on dietary exposure to AFT for the general population, compared with setting an ML of 15 µg/kg.	The CONTAM Panel acknowledges this comment. And as stated in Section 3.3.3. the assessment of the effect on public health of a possible change of MLs is outside the scope of the current Scientific Opinion.
	38	3.5.2 Exposure scenario/exposure model	Sorting and processing Lines 2685-2687: Processing was not considered in the dietary exposure assessment since the relevant information (e.g. milling, sorting, cleaning, heat treatment of cereals, roasting of nuts) was provided for only a limited number of samples. FRUCOM comment: the EFSA conclusion does not correspond to the business practice. The processors and traders of dried fruit and nuts attach great importance to aflatoxin control and reduction at all stages of the chain. For example, the fig processing involves minimum 2-3 controls of each fruit under long wave UV lights in the black room and then followed by private testing in the lab (sometimes twice) and finally by the official sampling and testing. "Sorting equipment is critical for the reduction of the levels of aflatoxins and substantial reduction is achievable due to sorting out of kernels, some of which will not be aflatoxin contaminated but will still be removed as a	Insufficient information was available in the EFSA Chemical Occurrence database to separate samples that were not subject to sorting or any other physical treatment from samples that are intended for direct human consumption. Therefore, all available samples were used in the exposure assessment. This may lead to an overestimation of the exposure. The text in the uncertainty section (3.5.2. and Table 21) has been updated to make this clearer.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			preventive measure. Blanching and resorting of nuts and peanuts is a common procedure; acknowledgement of the effectiveness of these treatments (90-95% reductions) is the basis for Codex and EU recognition of "further processing to reduce aflatoxin contamination" in the setting of limits as well as a means of reprocessing rejected consignments. T. B. Whitaker (1997) Eficiency of the Blanching and Electronic Color Sorting Process for Reducing Aflatoxin in Raw Shelled Peanuts. Peanut Science: January 1997, Vol. 24, No. 1, pp. 62-66. Additional unpublished studies on almonds by Dr. Whitaker. • Roasting resulted in aflatoxin reduction: o Ismail, A., Gonçalves, B. L., de Neeff, D. V., Ponzilacqua, B., Coppa, C. F., Hintzsche, H., ... & Oliveira, C. A. (2018). Aflatoxin in foodstuffs: Occurrence and recent advances in decontamination. Food Research International, 113, 74-85. o Martins, L. M., Sant'Ana, A. S., Iamanaka, B. T., Berto, M. I., Pitt, J. I., & Taniwaki, M. H. (2017). Kinetics of aflatoxin degradation during peanut roasting. Food research international, 97, 178-183. o Arzandeh, S., & Jinap, S. (2011). Effect of initial aflatoxin concentration, heating time and roasting temperature on aflatoxin reduction in contaminated peanuts and process optimisation using response surface modelling. International journal of food science & technology, 46(3), 485-491. o Yazdanpanah, H., Mohammadi, T., Abouhossain, G., & Cheraghali, A. M. (2005). Effect of roasting on degradation of aflatoxins in contaminated pistachio nuts. Food and Chemical Toxicology, 43(7), 1135-1139. • Food processing can further reduce mycotoxin levels by physical removal: o Karlovsky, P., Suman, M., Berthiller, F., De Meester, J., Eisenbrand, G., Perrin, I., ... & Dussort, P. (2016). Impact of food processing and detoxification treatments on mycotoxin contamination. Mycotoxin research, 32(4), 179-205. • TOMRA. Aflatoxin Whitepaper: https://food.tomra.com/aflatoxin-	

Stakeholder	Comment number	Chapter	Comment	EFSA response
			whitepaper-form?hsCtaTracking=2910f5f2-bca9-446f-8271-e81dbcd528e8%7Cdd06cec2-aa5e-4b63-9926-19dda3d00d8e#form Processors conduct substantial numbers of analysis of aflatoxins both prior to processing and after processing, and before shipment/on receipt of goods.	
	39	3.5.2 Exposure scenario/exposure model	Exposure scenario/exposure model FRUCOM comments relate to lines 2669-2679 of the draft opinion, in particular: The exposure assessment was based on aflatoxin occurrence data collected in numerous EU countries; however, most of them (~ 65%) were collected in only three Member States. The available occurrence data have been in part collected via a risk-based monitoring strategy and this may overestimate the background aflatoxin levels. FRUCOM comments: many main origins for the dried fruit, nuts and oilseeds are included in the Regulations 669/2009 and 884/2014 and are subject to compulsory checks at origin/on arrival in the range between 5% and 50% of goods supplied. This explains very high prevalence and skewed statistics for these categories of products in the tables 9 and 10. Since most of the testing results coming from Official Controls performed at the border and all non-compliant commodities are rejected, it means that consumer exposure to afla via nuts and seeds (including peanuts) is much lower – the established limits for aflatoxin in tree nuts is 10 ppb total / 8 ppb b1 and for peanuts is 4 ppb total / 2 ppb B1. The exposure data used by EFSA on levels of AF in foods came mostly from three countries, Germany, Netherlands, and France. This is very likely to be from RASFF/border rejections and enhanced controls which are disproportionately high. Importantly, the figures do not take into consideration that these data do not reflect what percentage of mandatory controls complied with EU regulatory limits, and were therefore allowed to enter the market. As a result, this has led to an overly conservative estimate.	The CONTAM Panel does not agree with the assumption that all samples on the market comply with the ML that is currently in place. In practice, a certain percentage of samples on the market will exceed the ML, and therefore, an underestimation of the risk is made when using the ML as cut-off value for occurrence data. Section 3.5.2. includes the following sentence: "*The available occurrence data have been in part collected via a risk-based monitoring strategy and this may overestimate the background aflatoxin levels*". The CONTAM Panel considers that it is sufficiently clear in the opinion.
	40	3.5.4 Other uncertainties	Toxicological studies Lines 2745-2747: Although the available evidence suggests differences in	The CONTAM Panel included the following sentence in Section 3.1.6.: "*The CONTAM Panel considers that this conservative*

Stakeholder	Comment number	Chapter	Comment	EFSA response
			potencies between AFB1, AFB2, AFG1 and AFG2, the available data do not make it possible to identify potency factors. The CONTAM Panel assumed equal potencies for the four compounds, which leads to an overestimation of the risk for AFT. FRUCOM comments: EFSA assumed the relative potency of aflatoxins B2, G1, G2 to be of equal potency to B1. This is a conservative assumption and EFSA acknowledged that it is likely to overestimate the risk: B1 and G1 are carcinogenic; there is limited evidence that B2 is carcinogenic and inadequate evidence that G2 is carcinogenic. In genotoxicity studies, all are less genotoxic compared to B1. EFSA concludes: "it is not appropriate to establish a tolerable daily intake" and that the estimated exposure to aflatoxin in food because of the Margin of Exposure, "raises a health concern." Not having a tolerable daily intake makes it harder to support standards. The MOEs are based on a $BMDL_{10}$ from a 45-year old study in rats. The Wogan et al. (1974) rat study was selected by EFSA as the pivotal study (3.1.5.2 Dose–response analysis) and it undoubtedly has limitations that are not identified in the EFSA draft. * The testing standards were very different in the early 70s when this study was conducted. * It may be worthwhile to do a critical evaluation of the Wogan et al. (1974) publication to identify possible uncertainties with the underlying data used by EFSA.	*approach is appropriate in this case, but notes the uncertainty arising from the insufficient data available on AFB2 and AFG2.*" AFB1 is carcinogenic via a genotoxic mode of action. This has been the conclusion of different risk assessments (see Section 1.3.3). It is widely accepted, and recommended by EFSA (EFSA, 2005) and WHO (WHO/IPCS, 2009), to apply a margin of exposure approach for compounds that are both genotoxic and carcinogenic. The CONTAM Panel notes that at the time of the Wogan study (1974) the OECD guidelines did not exist. The CONTAM Panel acknowledges that the description of this study is concise. This study has some limitations, but the CONTAM Panel considers that the strengths of the study outweigh these. Full histological examinations and detailed autopsies were performed. Highly purified crystalline AFB1 was used and diets were prepared under controlled conditions. A clear dose-response relationship was observed confirming previous reports of AFB1 as a potent liver carcinogen. No study performed in accordance with current OECD guidelines is available.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			EFSA assumes that the rat can accurately predict human risk – but rats and humans may not respond to aflatoxins in the same manner. * EFSA presented epidemiologic studies and implied that the risk assessment outcome is about the same whether the rats data or human data is used, which is probably an oversimplification. * For starters, most of the human data comes from studies of populations that are exposed to high levels of aflatoxins and have high rates of hepatitis B. * Rats may be similar to humans with hepatitis B, but humans with hepatitis B are 30 times more sensitive to aflatoxins than humans without hepatitis B. In the U.S., fewer than 1% of the population tests positive for hepatitis B. 2613. Overall, the prevalence of HBV and HCV in the EU/EEA was estimated to be around 0.9 and 1.1% Using the rat data may greatly overestimate the risk, and EFSA should at least acknowledge the uncertainty.	The use of rodent data in human risk assessment is a general practice used by different risk assessment bodies. The uncertainty linked to the use of rodents as a model for humans is taken into account by using the MOE approach. The MOE is not a direct measure of risk but is an expression of the level of concern.
			Lines 2721-2713: The cancer potencies were calculated by the JECFA for both HBsAg-positive and HBsAg-negative individuals. The cancer potency for HBsAg-negative individuals is based on relatively few cases and is therefore more uncertain than the estimated potency for HBsAg-positive subjects.	The CONTAM Panel acknowledges this comment.
			Aflatoxins were first evaluated at the 31st JECFA meeting in 1987, and at a number of subsequent meetings. JECFA noted in their 2007 evaluation that "results of studies relevant to a toxicological evaluation, particularly metabolic and epidemiological studies, published since the last JECFA risk assessment of AFL, did not alter that assessment and indeed lent support to the conclusions reached in that assessment." It is important to note that the 1974 Wogan study was among those included in the initial JECFA assessment.	The previous JECFA assessments were taken into account in the current opinion as explained in Section 1.3.3.
	41	4.0. Conclusions (overall chapter)	Conclusion - our position: • EFSA draft opinion presents no evidence to suggest there is an "additional consumer health risk" based on a single 1974 study which has been previously considered in global risk assessments for aflatoxin. • We support EFSA recommendations for further research on carcinogenicity of other aflatoxins especially AFB2 & AFG2, but do not believe the EFSA assessment should assume equivalent toxicity as a basis for this evaluation.	The CONTAM Panel is aware of the uncertainties in the risk assessment as described in Section 3.5 of its assessment. The CONTAM Panel encourages fit-for-purpose scientific research and data collection that would allow clarification of the uncertainties in the risk assessment of aflatoxins.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			• The EFSA opinion states it is an "overly conservative" estimation, and is based not on new exposure or potency data, but on a 45 year old study that was already included in established risk assessments. There is really no new scientific information presented that changes the existing risk assessment. • Research should be aimed at reducing uncertainty in risk assessment measurement. • Experimental or academic theorizing should not be basis of any new regulation without further evaluation of whether such a change presents a meaningful impact on consumer health or trade. • Occurrence data coming from rejected commodities at the border have to be separated from the data received during the market surveillance. The latter data should be used as basis to calculate the exposure. • Any proposed changes to analysis would need to be clearly researched first, analytical tool needs to be sufficiently available and at suitable cost to allow trade to be conducted without undue delay. • Sampling and sample preparation methods need to be thoroughly reviewed for potentials of false positives and false negatives before any changes to legislation are made. • We would also recall some recommendations by JECFA in 2017: The Committee recommends that efforts continue to reduce aflatoxin exposure using valid intervention strategies, including the development of effective, sustainable and universally applicable preharvest prevention strategies. Based on their contribution to dietary aflatoxin exposure in some areas of the world, rice, wheat and sorghum need to be considered in future risk management activities for aflatoxins.	
Human Biomonitoring Initiative (HBM4EU Initiative)	42	General comments	Mycotoxins' experts on HBM4EU (https://www.hbm4eu.eu/) congratulate CONTAM Panel for the very extensive and detailed work on this opinion and highlight its importance for the assessment of European population exposure to aflatoxins through food. The reference values generated by EFSA, especially BMDL10, are considered of great interest by the scientific community since they contribute to harmonize calculations allowing a harmonized approach for the characterisation of aflatoxins.	Regarding the selection of mycotoxins to be included in the HBM4EU, a prioritisation was needed since not all substances of interest could be included.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			EFSA recommendation on monitoring these toxins, "Aflatoxin occurrence should continue to be monitored in the light of potential increases due to climate change using methods with high levels of sensitivity for detection", is highly encouraged. HBM4EU is a project integrating 30 countries that aims to assess the exposure of European citizens to food chemicals through biomonitoring. During the 2nd round of substances, deoxynivalenol (DON) and fumonisin B1 (FB1) were considered the prioritized substances within mycotoxin group. Due to the results and expertise of Portugal and the Netherlands teams on this topic, aflatoxins were considered an important candidate to also join this substance group. However, aflatoxins were not included considering the view of the stakeholders involved (EU Policy Board, EFSA and DG SANTE). Therefore, this is a limitation to the potential contribution of HBM4EU regarding the recommendation of the scientific opinion, "A well-designed study measuring dietary exposure and biomarkers of exposure is required to quantify the relationship between biomarker levels and exposure at the individual level." Nevertheless, HBM4EU chemical group leaders for mycotoxins and mycotoxin group members under this project, working closely with the different work package leaders, will try to profit from the possible opportunities during data collection to try to contribute to fill this gap when possible.	
	43	Summary	-Line 92-95: "AF-alb (AFB1-lys), urinary AF-N7-gua and urinary AFM1 are all validated biomarkers of dietary exposure to aflatoxin. However, the levels of these biomarkers cannot be converted reliably into dietary exposures in individuals. As AF-alb (AFB1-lys) better reflects longer-term exposure (i.e. several weeks), it tends to be most widely used, while urinary AFM1 and AF-N7-gua are suitable biomarkers for recent exposure". Question/remark It is not clear what is meant with "validated" biomarkers. In the opinion no remark(s), criteria or definition has been given related to the classification of "validated". Furthermore, in section 3.1.3.1 (from lines 1329 onwards) the biomarkers AF-	The CONTAM Panel revised the text in Section 3.1.3.1. to explain what is meant by validation. Further changes were done in the summary and conclusions.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			alb (AFB1-lys), AF-N7-gua and AFM1 are discussed and this does not shed any light on the appropriateness of these biomarkers for the determination of dietary exposure. In this section it is mentioned that AF-N7-gua adducts in urine do not show a (strong) association with the dietary intake of AFB1 (lines 1342-1344) but a good correlation (line 1359) has been shown between dietary aflatoxin intake and AF-alb levels in adults in Gambia (correlation coefficient = 0.55; $p<0.05$) and children in Tanzania (correlation coefficient = 0.43; $p<0.01$). Further on (lines 1394-1396) it is mentioned that a correlation between urinary AFM1 levels and dietary intake of AFB1 in maize ($r = 0.442$, $p<0.001$), as well as between AFM1 in urine and AF-alb in serum of the children ($r = 0.468$, $p<0.001$) was observed. In lines 1400-1404 the quote above is mentioned again without mentioning why these biomarkers cannot be converted reliably into dietary exposures in individuals. In addition, in this respect, the term "biomarkers" should be "biomarkers of exposure". -Lines 143-145: "A well-designed study is required to quantify the relationship between biomarker levels and exposure at the individual level". Question/remark It is not explained what is mentioned with "a well-designed study". Obviously, a human intervention study where aflatoxin(s) would be administered to volunteers can be ruled out with respect to the carcinogenic property of the aflatoxin(s). The combination of a duplicate diet study in Europe with (24h) urine collection can also be ruled out because of the (extremely) low number of positive samples in either diet or urine. From a statistical point of view this would require an unacceptably large population to be studied. This means that probably an epidemiological study, like a (nested) case–control study, will have to be used and this type of study has already been evaluated in the EFSA opinion. Summarised, it would of (great) help if EFSA could explain in more detail was is meant with "a well-designed study". Note: the above-mentioned quotes are also summarised as bullets,	The CONTAM Panel revised the text at several places in Section 3.1.3.1. to improve clarity. The CONTAM Panel clarified this at the start of Section 3.1.3.1. The CONTAM Panel acknowledges that the phrasing was unclear and revised the text in the summary and the recommendation.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			respectively in the Conclusions lines 2794-2796 and Recommendations lines 2883-2884.	
	44	3.1.1 Toxicokinetics	Figure 1: Question/Remark Suggestion to improve quality of letters of this figure	Different font was used to improve the quality of the letters.
	45	3.3.4 Non-dietary sources of exposure	-Line 2569-2571: "While occupational exposure may contribute significantly for individual workers, this is not considered further in this Scientific Opinion". Question/remark Although this is not a topic for this opinion, it is proposed that a brief sentence could be added after this paragraph, since this is an important health impact topic revealing in some cases high levels of exposure to AFB1 (Appendix D, Table D1, line 3969) that is until now poorly studied and deserving particular attention. A suggestion is to added the following text: "However, due to its important consequences on health, climate change can also have an impact on workers exposure to AFB1 since in some occupational settings the handle of huge quantities of raw materials with higher AFB1 contamination (cereals, feed,..) will imply higher exposure of workers. In these cases, biomonitoring tools allow to evaluate workers exposure and to recognize what the workplace environment adds to the exposure occurring by food consumption, providing the information needed for defining the best risk management measures".	The CONTAM Panel acknowledges the comment. However, this is not in the scope of the opinion.
The Wonderful Company	46	Summary	Codex Alimentarius Discussions Underway. As pointed out in the Draft's Background [beginning on line 216], the Codex Alimentarius and specifically in the Codex Committee on Contaminants in Food (CCCF), discussions are underway on maximum levels (MLs) and an associated sampling plan for aflatoxins in different foodstuffs are ongoing. We recognize that Codex standards are important for international trade and are designed to be simultaneously health-protective and trade-inclusive at a global level. Furthermore, we believe that any future considerations of lowering MLs for the aflatoxins in the food products discussed in the Draft would offer little additional health protection, but instead would result in	The CONTAM Panel acknowledges the comment. For clarity, the draft opinion presented for public consultation is the comprehensive risk assessment that was recommended in 2018.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			greater rejections of affected products and have a negative impact on trade. We have been carefully tracking these developments over the years as they relate to our key products, almonds and pistachios, and we will continue to maintain our focus on these important developments as they relate to human health protection and world trade considerations. We are also in agreement with EFSA's plans to perform a comprehensive risk assessment related to the presence of aflatoxins in food.	
	47	1.0. Introduction (overall chapter)	The Wonderful Company LLC, on behalf of Wonderful Orchards ("WO") and Wonderful Pistachios and Almonds LLC ("WP&A") (collectively "Wonderful"), appreciates the opportunity to respond to the European Food Safety Authority Panel on Contaminants in the Food Chain's ("EFSA") request for comments on the draft scientific opinion on the risks to public health related to the presence of aflatoxins in food ("Draft"). WO and WP&A, together, are the world's largest vertically integrated grower and processor of pistachios and almonds. We maintain large, state-of-the art almond and pistachio processing and packaging facilities in California. WP&A distributes over 500 million pounds of pistachios and 80 million pounds of almonds to our customers annually throughout the world. We have a long record of producing safe and high-quality nut products and are dedicated to the safety of our consumers worldwide. Wonderful recognizes how important the Draft is to public health and appreciate EFSA's role in helping the food industry deliver safe food products to European consumers. We further appreciate that the Draft presents no evidence to suggest that aflatoxin limits should be lowered and support EFSA's recommendations for further research on carcinogenicity of other aflatoxins especially AFB2, AFG1 and AFG2. We consider it important that stakeholders have the opportunity to review and address EFSA's final recommendations or requirements prior to making any changes to the legislation. We appreciate the opportunity to provide these comments and are available should EFSA require additional input or information.	The CONTAM Panel acknowledges this comment.
	48	1.3.3. Previous assessments 3.1.2 Toxicity in experimental animals	Aflatoxin Biomarkers, Specifically the AFB1-Lysine Adduct of Serum Albumin As pointed out by Vidal et al. (2018) (not cited in the Draft) in their comprehensive review of mycotoxin biomarkers, the use of biomarkers has become generally accepted, and biomarker-driven research has been	The CONTAM Panel is aware of the review by Vidal et al. (2018), which does not provide new information that is not already included in the opinion. The paper describing the LC-

Stakeholder	Comment number	Chapter	Comment	EFSA response
		3.1.3 Observations in humans	proposed as a successful method to assess the exposure to xenobiotics by using concentrations of the parent compounds and/or metabolites in biological matrices such as urine or blood. However, while the identification and validation of biomarkers of exposure remain a challenge, recent advances in high-resolution mass spectrometry (HRMS) along with new analytical (post-acquisition data mining) techniques can improve the quality and output of the biomarker identification process. While chronic daily or even acute exposure to numerous mycotoxins remains a fact, it is crucial that metabolism of the mycotoxins is unravelled so that more knowledge on biomarkers in humans and animals is acquired. Vidal et al. (2018) aimed to provide the scientific community with a comprehensive overview of reported in vitro and in vivo mycotoxin metabolism studies in relation to biomarkers of exposure for various mycotoxins (including the aflatoxins), so it would be a helpful addition to the Draft. Vidal et al. (2018) were careful to point out on several pages of their review that the AFB1-lysine (AFB1-lys) adduct of serum albumin is the most reliable biomarker of chronic aflatoxin exposure in plasma, and they cited several recently published studies in rats, swine and humans to support their contention (Di Gregorio et al., 2017; McMillan et al., 2018; Xue et al., 2016) (these papers were not cited in the Draft, while earlier ones were). The Draft correctly cited Guengerich et al. (2002) as one of the earliest papers describing this adduct. In fact, McMillan et al. (2018) used LC-HRMS in combination with isotope dilution MS to quantify AFB1-lysine, again citing this adduct as the most reliable biomarker of chronic aflatoxin exposure. Importantly, this is the first report where HRMS is used to quantify aflatoxin biomarkers in a human case-control study design, which is a promising research trend that should be stressed in the Draft. While the Draft in several places does discuss this important biomarker adduct and its fairly wide usage as a measure of longer-term aflatoxin exposure (e.g., several weeks), it fails to stress this adduct as the most reliable one. Additionally, the Draft does not mention that this albumin adduct, AFB1-lysine, actually represents a biological sink that serves to remove aflatoxin metabolites from the animal and human circulation, thus reducing the probability that genotoxic aflatoxin metabolites will be bioavailable to eventually reach target liver DNA-reactive sites. This same lack of recognition that the formation of adduct-protein AFB1-lysine represents a reduced risk of the carcinogenic potential of the aflatoxins, also plagues the extensive	HRMS method (McMillan et al., 2018) has been added to Section 3.1.3.1. The suggestion that "AFB1-lysine represents a biological sink that serves to remove aflatoxin metabolites from the animal and human circulation" is not supported currently by evidence from the literature.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			literature on the acrylamide-hemoglobin adduct. The hemoglobin adduct of acrylamide is also correctly acknowledged as the most reliable biomarker of acrylamide exposure, but it rarely receives the recognition that its formation represents a carcinogenic risk reduction, just as with AFB1-lysine formation.	
	49	3.1.4 Mode of action 3.1.5 Considerations of critical effects and dose–response analysis	Higher Carcinogenicity Impact of the Aflatoxins in HBV and HCV-Infected Populations. We agree with the CONTAM Panel's assessment that the weight of the evidence strongly demonstrates that aflatoxin exposure is associated with a higher human risk of developing hepatocellular carcinoma [HCC] in people infected with either HBV or HCV, providing one mechanistic basis for such a risk of liver cancer. However, we believe the importance of this co-exposure could be much better emphasized in the Draft, pointing out that people who are not infected with HBV or HCV have a much lower risk of developing liver cancer due to their low-level exposure to various aflatoxins in their diets.	People who are not infected with HBV or HCV have a lower risk of developing liver cancer compared to people infected with HBV or HCV at a similar level of exposure. This has been addressed at several places in the opinion and the CONTAM Panel considers that it is sufficiently clear. This information is available in Sections 1.3.3., 3.1.3.2., 3.1.4.6.1. and 3.1.5, as well as in the summary and conclusions.
	50	3.3.1 Current dietary exposure assessment	Concentrations of Aflatoxin B1 in Almonds, Pistachios and Other Seeds vs. the Magnitude of Dietary Contribution of these Products to Total AFB1 Exposure. The Draft discusses the assessment of the chronic dietary exposure to various aflatoxins based on the very large dataset of over 210,000 analytical results from almost 70,000 samples. It was pointed out that the highest AFB1 and AFT mean concentrations were obtained for the food category 'legumes, nuts and oilseeds' (in particular for pistachios, peanuts and 'other seeds'), but peanuts were noted to be the highest contributor to dietary exposure among these products. In addition, despite the relatively high AFB1 concentrations measured in almonds, pistachios and other seeds, the total dietary exposure to AFB1 from these foods was small, which is explained by their low consumption compared to peanuts within this food grouping. Furthermore, "legumes, nuts and seeds' are much smaller dietary contributors to AFB1 intake than grains and grain-based products, which were described in the Draft as the most important contributors to AFB1 intake in all age classes.	The CONTAM Panel acknowledges the comment.
AEGEAN EXPORTERS ASSOCIATIONS	51	General comments	Please find enclosed documents for future works.	The CONTAM Panel thanks the stakeholder for providing this information.

Stakeholder	Comment number	Chapter	Comment	EFSA response
European Snacks Association	52	3.2 Occurrence data	**Data and exposure** Line 2124-2125: Considering the large amount of left-censored data present in the data set (around 90%), the presence of relatively high LODs/LOQs may have a significant influence on the UB scenario. Line 2200: Table 9: Summary of the AFB1 occurrence data by food category (µg/kg) Line 2670-2680: The exposure assessment was based on aflatoxin occurrence data collected in numerous EU countries; however, most of them (~ 65%) were collected in only three Member States while some other countries submitted only a limited number of data. Most of the imported foods, such as nuts and fruits, were sampled in harbour areas and afterwards transported throughout Europe, therefore it is believed that the data for these foods properly covers the EU market. The available occurrence data have been in part collected via a risk-based monitoring strategy and this may overestimate the background aflatoxin levels. ESA comments on the above: Most data on AFT occurrence on nuts seem to come from official controls performed at the borders. Many main origins of nuts and peanuts are subject to increased checks according to Regulations 669/2009 and 884/2014, ranging from 5% to 50% of consignments. Moreover, some national authorities and/or specific ports apply stricter policies (e.g. systematically testing the next 10 consignments from the same company/origin after a positive results) which lead to a high amount of data that is not representative of the actual AFT levels that can be found on the market – not only statistics may be skewed by the high amount of targeted controls, but some of these positive results lead to border rejections (i.e. nuts never entering the EU market) or reprocessing aimed to reduce AFT levels. This does not take into consideration the total number of consignments received/inspected, and therefore is not a true representation of consumption levels. Besides, a very high amount of data (86%) on 'Legumes, nuts and oilseeds' is left-censored. Therefore, we agree that the available occurrence data do indeed overestimate the actual AFT levels in final products. In our opinion, occurrence data should be based on final products as available on the market.	Insufficient information was available in the EFSA Chemical Occurrence database to separate samples that were not subject to sorting or any other physical treatment from samples that are intended for direct human consumption. Therefore, all available samples were used in the exposure assessment. This may lead to an overestimation of the exposure. The text in the Uncertainty Section (3.5.2. and Table 21) has been updated to make this clearer.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	53	3.2 Occurrence data	**Sorting and processing** Line 2300-2303: 3.2.3 Processing Food processing may influence the concentration of aflatoxins in food products. Milling of cereals distributes the aflatoxins among the different milling products but does not destroy them. Grain sorting and cleaning, on the other hand, may lead to a reduction by the removal of contaminated kernels. Line 2415-2419: Another very important contributor to the overall LB mean chronic dietary exposure to AFB1 was the food category 'legumes, nuts and oilseeds' (contributing up to 34% for the elderly). In most surveys, this high contribution was driven by peanuts (up to 23% in adults). Despite relatively high AFB1 concentrations measured in almonds, pistachios and other seeds, the exposure to AFB1 from these foods was small, which is explained by low consumption. Line 2685-2687: Processing was not considered in the dietary exposure assessment since the relevant information (e.g. milling, sorting, cleaning, heat treatment of cereals, roasting of nuts) was provided for only a limited number of samples. ESA comments on the above: Processing seems not to have been sufficiently taken into account in the exposure estimations. For instance, most peanuts sold on the market (either ready-to-eat or as ingredients) are blanched. One of the purposes of blanching (removal of the skin (testa) covering the kernel) is to make more visible the kernel defects allowing to reduce aflatoxin content thanks to the use of electronic colour sorting equipment to detect and reject peanuts that may contain aflatoxin and/or damage. The proportion of removed peanuts varies depending on the aflatoxin and damage load pre-blanching - typical values are 2-25%. Aflatoxin can reside on the testa and/or in the individual cotyledons. In some cases, removing the skins will typically reduce the level of detectable aflatoxin; some other times, it will be also necessary to remove both the skins and the affected kernels/splits to effectively reduce the level of detectable aflatoxin. Occurrence data from official controls performed at the borders are unlikely to take this reduction into consideration.	Insufficient information was available in the EFSA Chemical Occurrence database to separate samples that were not subject to sorting or any other physical treatment from samples that are intended for direct human consumption. Therefore, all available samples were used in the exposure assessment. This may lead to an overestimation of the exposure. The text in the Uncertainty Section (Section 3.5.2. and Table 21) has been updated to make this more clear.
	54	3.5 Uncertainty analysis	Risk assessment	The CONTAM Panel agrees that the approach is conservative as discussed in the

Stakeholder	Comment number	Chapter	Comment	EFSA response
			Line 2745-2747: Although the available evidence suggests differences in potencies between AFB1, AFB2, AFG1 and AFG2, the available data do not make it possible to identify potency factors. The CONTAM Panel assumed equal potencies for the four compounds, which leads to an overestimation of the risk for AFT. Line 2721-2723: The cancer potencies were calculated by the JECFA for both HBsAg-positive and HBsAg-negative individuals. The cancer potency for HBsAg-negative individuals is based on relatively few cases and is therefore more uncertain than the estimated potency for HBsAg-positive subjects. EFSA's approach is based on a conservative assumption that is likely to overestimate the risk for consumers. According to the available literature, B1 and G1 are found to be carcinogenic but there is limited evidence concerning carcinogenicity of B2 and G2. In genotoxicity studies, all of them are found to be less genotoxic than B1. The MOEs are based on a BMDL10 from Wogan et al. (1974) rat study, which was carried out 45 years ago with very different testing standards, assumptions and uncertainties which may not have been sufficiently taken into account. The response to aflatoxins in humans and rats may differ significantly. Also, most of the human data used in the study refer to populations that are both exposed to high levels of aflatoxins and have high rates of hepatitis B.	Uncertainty Section (3.5.4). In addition, the CONTAM Panel included the following sentence in Section 3.1.6.: "*The CONTAM Panel considers that this conservative approach is appropriate in this case, but notes the uncertainty arising from the insufficient data available on AFB2 and AFG2*." The CONTAM Panel notes that at the time of the Wogan study (1974) the OECD guidelines did not exist. This study has some limitations, but the CONTAM Panel considers that the strengths of the study outweigh these. Full histological examinations and detailed autopsies were performed. Highly purified crystalline AFB1 was used and diets were prepared under controlled conditions. A clear dose-response relationship was observed confirming previous reports of AFB1 as a potent liver carcinogen. No study performed in accordance with current OECD guidelines is available. The use of rodent data in human risk assessment is a general practice used by different risk assessment bodies. The uncertainty linked to the use of rodents as a model for humans is taken into account by using the MOE approach. The MOE is not a direct measure of risk but is an expression of the level of concern.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			We would also like to refer to previous assessments carried out by JECFA, namely the most recent impact assessment of different MLs for ready-to-eat peanuts, which concluded that 'enforcing a maximum limit (ML) of 10, 8 or 4 µg/kg for ready to-eat peanuts would have little further impact on dietary exposure to AFT for the general population, compared with setting an ML of 15 µg/kg. At an ML of 4 µg/kg, the proportion of the world market of ready-to-eat peanuts rejected would be approximately double the proportion rejected at an ML of 15 µg/kg (about 20% versus 10%).'	The CONTAM Panel acknowledges this comment. However, the assessment of the effect on public health of a possible change of MLs is outside the scope of the current Scientific Opinion.
European Dairy Association (EDA)	55	General comments	1. The importance of controlling aflatoxin in the food chain The dairy sector acknowledges the importance of controlling aflatoxin, which is a key issue for a responsible and safe manufacturing of dairy products. The occurrence is adequality controlled and verified by the monitoring of both feed and food to fulfil the EU maximum limits. 2. The aflatoxin levels presented in the draft opinion are higher than the levels found in monitoring programs The aflatoxin levels mentioned in the EFSA opinion are higher than recognised by our members. In the monitoring of a large number of samples for the past years, no detectable levels of aflatoxin have been found in raw milk or finished dairy products. Actually, in most cases the level of Aflatoxin M1 is more than 5 times lower than the EU ML. Thus, the values found in monitoring programs seem to be in contradiction with the occurrence data in the draft opinion. 3. Remarks about milk and dairy based products as a main source of aflatoxin M1 may be easily misinterpreted The conclusion that milk and dairy based products are the major contributors to exposure of aflatoxin M1 might be misinterpreted. Aflatoxin B1 is converted by the ruminant animal to Aflatoxin M1 and therefore milk is by nature the only source of aflatoxin M1. For outsiders, it may seem that milk is a high-risk product, whereas is it is simply the only product in which aflatoxin M1 naturally can be but rarely is present.	The CONTAM Panel acknowledges the comment EFSA invites EDA to submit the occurrence data via the call for data in 2020 so that the data can be used for future risk assessments. The following sentence is included in Section 1.3: "*Aflatoxins M1 (AFM1) and M2 (AFM2) are the hydroxylated metabolites of AFB1 and AFB2 and are found in milk and dairy products obtained from livestock that have ingested contaminated feed*". Therefore, the CONTAM Panel considers that no further changes to the opinion are necessary.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	56	3.2.1 Occurrence data on food as submitted to EFSA 3.2.2 Levels of biomarkers of exposure in the European population	There is an issue with the different words Appendix and Annex, which can be considered to be identical, thus creating confusion in the reading of the tables (esp. when a quick research for e.g. 'table D.2' is done). Example: Line 2285/2286 refers to Annex D Table D.2 which corresponds with regular farming versus organic farming. While later in line 2294/2295 the reference is to the Appendix D Table D.2 which corresponds with human milk. When checking Appendix D Table D.2, which is placed in the document itself, the table D.2 indeed refers to human milk; when downloading the Annex D in excel from the EFSA website and check table D.2 it indeed refers to regular versus organic farming. Would there be any way to prevent the confusion, even if things are correct?	The use of Annexes and appendixes is general practice in EFSA. An annex is a stand-alone document that offers additional information to the main text. An appendix may contain data and analyses that are considered too detailed to be included in the main text of the document. Its aim is to give greater details, tables, visuals or examples for better understanding of the main text. EFSA understands that using the same numbering for Annexes and Appendices may be confusing for the reader and revised the numbering of the Appendices by using roman numerals instead of letters.
National Institute for Public Health and the Environment (RIVM)	57	General comments	- RIVM would like to compliment CONTAM on the work done and would like to provide the comments below to facilitate the finalisation of the opinion.	Thank you
	58	2.3.2 Data analysis	lines 538-544 state 'The outcome of the data analysis is presented in Section 3.1.2'. Paragraph 3.1.2 however does not contain information on data analysis, but information on toxicity in experimental animals. CONTAM is requested to add the paragraph with data analysis information and refer to this correct paragraph. lines 545-556: CONTAM states "The left-censored data (results below the LOD or below the LOQ) were treated by the substitution method as recommended in 'Principles and Methods for the Risk Assessment of Chemicals in Food' (WHO/IPCS, 547 2009)". The same method is indicated in the EFSA scientific report 'Management of left-censored data in dietary exposure assessment of chemical substances' (EFSA, 2010b) as an option for the treatment of left-censored data. RIVM suggests to indicate that only for AFB1 and AFM1 left-censored data the	Indeed, the outcome of the data analysis is presented in Section 3.2.1. This has been corrected in the opinion. The substitution method was applied only to individual aflatoxins (AFB1, AFB2, AFG1 and AFG2) while for the AFT a specific approach was followed. The CONTAM Panel clarified this in Section 2.3.2.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			guidance EFSA (2010b) was followed. lines 557-564. It is unclear how occurrence data on AFB1 only were handled in the exposure assessment. CONTAM is requested to provide an explanation on how AFB1 exposure was calculated, i.e. was exposure for AFB1 calculated with samples only analysed for AFB1 or were they mixed with samples also analysed for other aflatoxins? lines 557-571: For the UB scenario CONTAM deviates from EFSA (2010b) and describes a different method in which the LOD/LOQ for AFB1 is used, under certain conditions described under bullets 2 and 3 on page 20, for substitution of left-censored data all other subtypes in the AFT scenario. CONTAM explains that 'AFB1 aflatoxin is the most frequently found and at the highest concentration, and that not all aflatoxin-producing moulds produce all four aflatoxins. Therefore, simply adding the four LODs/LOQs for samples in which none of the aflatoxins are quantified, would overestimate the UB AFT level'. RIVM agrees that imputation of left-censored data with LOD/LOQ in the UB scenario leads to very conservative exposure estimates, and could in principle agree with using an adapted approach. However, RIVM wonders if such an approach should be harmonized across opinions. Would EFSA consider adding this adapted approach to the existing guidance (EFSA, 2010)?	The mean concentration of any aflatoxin for a given food was calculated based on the analytical results from all samples analysed for that aflatoxin. This information was added to Section 2.3.2. The CONTAM Panel applied this approach as it is known for aflatoxins that AFB1 is the major contributor to the concentration of AFT. EFSA will consider this when updating the guidance dealing with handling of the (left-censored) data used for exposure assessment.
	59	2.6 Exposure assessment	lines 638-648. Cereal-based food is corrected when consumed with water or milk (different corrections). It is unclear which information allows CONTAM to do so. There is no reference provided. CONTAM is requested to provide an explanation on how it is decided when corrections should be made and, in case of correction, whether to correct with either water or with milk? lines 649-655: CONTAM Panel considered that it is of interest to also estimate a short-term exposure and estimated the short-term exposure to AFB1 among peanut butter consumers. The acute exposure estimate to AFB1 for peanut butter only clearly underestimates the potential high acute aflatoxin exposure	The data provider indicates whether the product is reconstituted with milk or water. This information has been added to Section 2.6. The CONTAM Panel concluded in Section 3.1.2.5. that "*AFB1 affects reproductive and developmental parameters at low doses in*

Stakeholder	Comment number	Chapter	Comment	EFSA response
			in consumers, as the background AFB1 chronic high exposure (all products) is much higher (see NL toddlers). Could CONTAM clarify why acute exposure from only peanut butter is used for the acute risk assessment? RIVM would suggest to perform an acute exposure assessment for all products. Could CONTAM clarify why the acute exposure was assessed only for AFB1 and not for AFT, does this relate to the fact that the acute effects is found for AFB1 only (see also comments on paragraph 3.1.2.5)? RIVM suggests that in future evaluations, acute exposure is assessed using probabilistic methods which have been developed in the area of pesticides.	*rodents and these effects may occur following a short-term exposure*". To evaluate whether these effects should be considered in the risk characterisation of aflatoxins in humans, the CONTAM Panel compared the identified doses with a scenario of short-term exposure before embarking on a resource-intensive probabilistic dietary exposure assessment. Peanut butter was selected since this has a relatively homogenous AFB1 concentration and somebody may be exposed for a short term to the same AF exposure, while in other foods, such as nuts or dried fruits, the contamination is more heterogenous. The short-term exposure to AFB1 was assessed since the reproductive and developmental effects were studied for this aflatoxin only. The text in Sections 2.6 and 3.3.1.3. were revised to improve clarity.
	60	3.1 Hazard identification and characterisation	In the draft opinion the CONTAM panel gives relatively concise description of the acute toxicity of aflatoxins, as more studies on acute toxicity are available (suggestions could be provided by RIVM). The acute toxicity of aflatoxins could, however, be of significant importance considering the possibility of acute high exposure due to contaminated batched of products (for example peanuts) and potential acute toxic effects of aflatoxins (see references below). The EFSA CONTAM panel is therefore requested to describe the acute toxic effects of aflatoxins more in depth, especially the selection of literature, and add an acute risk (hazard) assessment to the opinion.	The CONTAM Panel would like to thank RIVM for providing the list of papers not included in the opinion published for public consultation. The papers by McKean et al. (2006a and 2006b), identifying an oral LD_{50} value of 2.7 mg/kg bw for AFB1, were added to Section 3.1.2.1. However, this Scientific Opinion is an update of the Scientific Opinion on the potential increase of consumer health risk by a possible increase of the existing MLs for aflatoxins in almonds, hazelnuts and pistachios and derived products adopted by the CONTAM Panel of EFSA in January 2007 (EFSA, 2007a). Therefore, papers published from 2006 onwards were taken into account for the current risk assessment when not yet included in the previous opinion. This information has been added to Section 1.2.

Stakeholder	Comment number	Chapter	Comment	EFSA response
				Section 3.1.3.2.2. describes acute toxicity in humans (aflatoxicosis) caused by AFB1. The aflatoxin contamination levels reported in cases of aflatoxicosis are far higher than any seen in the EU, and the CONTAM Panel therefore considers the risk of aflatoxicosis to be highly unlikely in the EU. Establishing a HBGV, such as an ARfD, is not appropriate for genotoxic and carcinogenic substances.
	61	3.1.2 Toxicity in experimental animals	Table 3, paragraph 3.1.2.4. In the critical study (Wogan et al. 1974) used for deriving the BMDL for chronic risk assessment apparently relatively few animals have been exposed per dose-group, considering that at least 50 animals per sex per dose-group are required in guideline studies. Although fewer animals per dose-group would only result in a wider BMD CI, and thus a lower BMDL, the low number of experimental animals is not being discussed by the EFSA. In addition, only male rats were used, the description of the methods and results is very concise, the exposure duration is different for different dose groups, to name but a few shortcomings, which could have implications for the acceptability of this study. Could EFSA discuss why, in spite of the poor quality of the (reporting of) the study, the study is still considered acceptable for deriving a BMDL to be used in the risk assessment of aflatoxins.	The CONTAM Panel notes that at the time of the Wogan study (1974) the OECD guidelines did not exist. The CONTAM Panel acknowledges that the description of this study is concise. This study has some limitations, but the CONTAM Panel considers that the strengths of the study outweigh these. The CONTAM Panel added the following text to Section 3.5.4.: "*Despite the fact that this study was carried out before OECD test guidelines were put in place, full histological examinations and detailed autopsies were performed. Highly purified crystalline AFB1 was used and diets were prepared under controlled conditions. A clear dose-response relationship was observed confirming previous reports of AFB1 as a potent liver carcinogen. No study performed in accordance with current OECD guidelines is available.*"
			In the study critical study used for deriving the BMDL (Wogan et al., 1974) the different dose-groups have different durations of exposure, i.e. the higher the dose, the shorter the treatment duration. This leads to the questions on what the tumor incidence would have been for the higher dose-groups, had	The uncertainty due to time adjustment is described in Section 3.5.4.: "*However, a BMD analysis of the non-adjusted doses resulted in the same $BMDL_{10}$ value of 0.4 µg/kg bw per day (when rounded to one*

Stakeholder	Comment number	Chapter	Comment	EFSA response
			they had a longer duration of exposure. A different tumour incidence could result in a different BMDL. In order to compensate for the shorter treatment duration in the treatment groups EFSA performs a time-adjustment for the doses. The methodology used is however not being explained in much detail. Also, a linear time adjustment is performed, which is not realistic for the development of tumours that usually develop exponentially (over time). Could EFSA elaborate on the potential underestimation of the carcinogenic potency due to the assumption of linearity in the tumour incidence over time? 3.1.2.5. lines 1231-1241. For acute risk assessment EFSA uses the effects observed in a 28-day study by Hasanzadeh & Rezazadeh (2013) on spermatogenic cells in rats. The study shows that exposure to AFB1 leads to adverse effects on the spermatogenesis and reports a LOAEL of 4 µg/kg bw per day in rats (3.1.5.1, 2043-2050). Effects at the lowest dose are a ± 20% reduction in spermatogonia type A and B distribution at 0.1 mm2 of seminiferous tubular tissue in control and ± 50% reduction in spermatozoa distribution at 0.1 mm2 of seminiferous tubular tissue. EFSA concludes in 3.1.5.1 that the calculated acute exposure of humans is three orders of magnitude lower than the LOAEL of 4 µg/kg bw per day, and therefore that reproductive and developmental toxicity is not the critical endpoint for a risk assessment. RIVM has a number of comments and questions concerning this acute risk assessment. RIVM agrees with EFSA that the effects on spermatogenic cells, although observed in a repeated dose study, may be relevant for an acute risk assessment, as these effect may already have been caused by a single exposure. As this may not be clear to the reader could EFSA give a justification why this	*significant number; data not shown) as when time-adjusted doses were used. Therefore, the uncertainty caused by the time adjustment is low."* The time-adjustment is described in Section 3.1.2.4 and more precisely in footnote 17 to the text and footnote c of Table 3. Evidence from studies in rainbow trout indicate a linear dose-response as described in Sections 3.1.2.4 and 1.3.3. The CONTAM Panel described all available studies and assessed whether these studies were critical for risk assessment. The Panel concluded that the study by Hasanzadeh & Rezazadeh (2013) is not a pivotal study for risk assessment. Establishing a HBGV, such as an ARfD, is not appropriate for genotoxic and carcinogenic substances. No information is available on the mode of action regarding the effects on spermatogenic cells for aflatoxins. Therefore, performing a read-across from AFB1 to other aflatoxins would be speculative. The CONTAM Panel agrees that the selection of a critical effect is not dependent on the actual exposure. The text in Section 3.1.5.1. was modified.

Stakeholder	Comment number	Chapter	Comment	EFSA response
			(sub)chronic study was deemed fit to serve as a critical study for assessing the risks of acute exposure? In the study there was no NOAEL for the effects on spermatogenic cells. § Could EFSA perform a BMD analysis on the data, in order to perform an acute risk assessment? § If so, could EFSA indicate what it considers to be the critical effect sizes (% change from control in the measured parameters) for the observed effects? § If the data do not allow a BMD analysis, could EFSA indicate what the appropriate assessment factor would be for the extrapolation from the LOAEL to an NOAEL, taking into account the high effect sizes at the LOAEL? § Does EFSA consider, as a conservative approach, that the effects on spermatogenic cells could also be induced by other aflatoxins than AFB1? § Could EFSA explain why selection of a critical endpoint is dependent on actual exposure, as usually the POD is determined as a separate risk assessment step? § Would EFSA consider it appropriate to establish an ARfD based on the effects on spermatogenic cells? § Could EFSA provide the actual calculated MOE or the exposure expressed as percentage of ARfD, rather than indicating the orders of magnitude that the exposure differs from the PoD?	
	62	3.1.5 Considerations of critical effects and dose–response analysis	o [section 3.1.5.2, lines 2085-2091] In the draft opinion EFSA (lines 2085-2091) regards the study of Yeh et al. (1989) as a pivotal study. However, after analysis the BMDL of this study is not used because the BMD CI is considered too wide. For details of the BMD analysis the EFSA draft opinion refers the reader to EFSA CONTAM, 2018. EFSA CONTAM, 2018 does not provide details about the BMD analysis of the Yeh et al. dataset (only some plots in appendix B). No underlying (dose-response) data, BMD CI and methods are reported. Instead, the reader is referred to FAO/WHO, 2017. In FAO/WHO, 2017 a dose-response analysis based on the data of Yeh et al. is performed, however underlying (dose-response) data, BMD CI and methods	The underlying dose-response data are shown in Table 5 of the current draft opinion. The CONTAM Panel considered that it is sufficiently clear from the graphs shown in appendix B of the 2018 opinion, that a very small trend in the dose–response curve was observed for HBsAg-negative subjects. The appendix B of the 2018 opinion also specifies the models that were used and are

Stakeholder	Comment number	Chapter	Comment	EFSA response
			are not reported. In EFSA, 2007 (table 45; doi:10.2903/j.efsa.2007.446), dose-response data of Yeh et al. are presented. However, to facilitate dose-response analysis, one would also need the total group sizes of HBsAG- and +. It is unclear if EFSA CONTAM, 2018 analyzed this data (PLC cases or APY, and with what group sizes?). All in all, it remains unclear what data are analyzed, which method was used and which results were obtained. Due to the lack of information, the statement that the BMD CI is too wide and cannot be used cannot be substantiated.	the same as used by the JECFA (FAO/WHO, 2018).
			We would suggest that EFSA provides the details on the dose-response analysis of the Yeh et al. (1989) data in a similar fashion as the details provided of the dose-response analysis of the Wogan study (appendix C). This would also be in line with the guidance on reporting of a BMD analysis (section 2.5.9 in Update: Guidance on the use of the benchmark dose approach in risk assessment. EFSA Journal 2017;15(1):4658, 41 pp. doi:10.2903/j.efsa.2017.4658).	An attempt was made to explore possible BMRs for calculating BMDLs. Due to the shallow dose–response curve for HBsAg-negative subjects, no meaningful BMDL could be calculated. These results were not included in the opinion.
			o [section 3.1.5.2] A wide BMD CI is an indication of poor data (or a too small BMR, but this is not the case here). The conclusion in the draft EFSA opinion that the data of Yeh et al. (1989) result in a BMD CI which is too wide automatically leads to the conclusion that the data of Yeh et al. are of poor quality. Could EFSA provide an explanation on the reason why the Yeh et al. data are considered not of sufficient quality to derive a BMDL, but are considered sufficiently good to derive cancer potencies.	The CONTAM Panel is aware of this limitation of the data and this is described in the uncertainty section. Considering the uncertainties in both the human and animal data, both lines of evidence were therefore used in the risk characterisation.
			o [section 3.1.5.2, lines 2085-2091] FAO/WHO derived their cancer potencies using restricted dose-response models. The EFSA BMD guidance explicitly states that constraints should not be used. Only using constrained models may result in an overestimation of the BMDL (and underestimation of the cancer potency). RIVM suggests to re-analyse the Yeh et al. data using unrestricted models (provided that the previous comment on the quality of the Yeh et al. data is sufficiently addressed).	The modeller that calculated the cancer potencies at the 83rd JECFA meeting confirmed that JECFA used models without restricting the steepness parameter (Wheeler, 2019 personal communication).
			o [section 3.1.5.2, lines 2085-2091] In the Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for Risk Assessment of Substances Which are both Genotoxic and Carcinogenic (EFSA Journal (2005) 282, 1-31), EFSA stated that "In an attempt to extrapolate from the high doses in animal studies to the lower levels to which humans are exposed, a wide range of models from simple linear extrapolation	The 2005 opinion describes the methodology for risk characterisation of genotoxic and carcinogenic substances when using animal data (EFSA, 2005); this guidance was followed and the MOE approach was applied

Stakeholder	Comment number	Chapter	Comment	EFSA response
			to very complex ones have been developed and used. This has resulted in differing conclusions for the same substance, depending on the model chosen. Moreover, for any particular substance, it is not known whether or not the model chosen actually reflects the underlying biological processes. The Scientific Committee therefore recommends using a different approach, known as the margin of exposure (MOE) approach." EFSA is requested to include a reasoning in the draft aflatoxin opinion why for the human studies a deviation was made from this 2005 opinion? o [section 3.1.5.2, lines 2085-2091] Cancer potencies assume a linear dose response. Can you provide any evidence that the dose-response of the Yeh et al. data, or any other cancer dataset, is indeed linear (on the appropriate log-dose scale)? If this is not possible, please discuss the validity of applying the cancer potency approach.	to the data from Wogan et al. (1974). The 2005 opinion does not cover the use of human data. Therefore, the CONTAM Panel is not deviating from the 2005 opinion. In accordance with JECFA, the CONTAM Panel considered the application of potency estimates as appropriate as extrapolation far outside the observable range was not needed. The lowest observed dose was 12 ng/kg bw per day (see Table 5) and extrapolation was done to 1 ng/kg bw per day. This is explained in section 1.3.3 by the following text: "*Rainbow trout exposed for four weeks showed a hepatotumourigenic response over a dose-range of 0.05–110 µg/kg diet after one year (Williams et al., 2009, Williams, 2012). The JECFA (FAO/WHO, 2018) noted that the dose-related tumourigenesis did not seem to deviate from a log-linear relationship and that a similar relationship was observed between the dose of AFB1 and AFB1–DNA adducts in trout and rat liver (Bailey et al., 1998; Pottenger et al., 2014). These observations with doses approaching human exposures lend support to the application of a linear non-threshold model in AFB1 cancer risk assessment.*"
	63	3.2.1 Occurrence data on food as submitted to EFSA	lines 2144-2146. The exposure relies on German, Dutch and French occurrence data, this might have a high impact on uncertainty for the remaining MS. It is not being discussed whether the occurrence data represent data from other MS. RIVM suggests that CONTAM discusses the uncertainty caused by using mainly the occurrence data of three Member States.	The following text is included in Section 3.5.2. Exposure scenario/exposure model: "*The exposure assessment was based on aflatoxin occurrence data collected in numerous EU countries; however, most of them (~ 65%) were collected in only three Member States while some other countries submitted only a limited number of data. Most of the imported*

Stakeholder	Comment number	Chapter	Comment	EFSA response
				foods, such as nuts and fruits, were sampled in harbour areas and afterwards transported throughout Europe, therefore it is believed that the data for these foods properly covers the EU market. This seems not to be the case for the other food categories largely contributing to the exposure to aflatoxins, in particular 'grains and grain-based products' and 'milk and milk products'. For these food categories, there is uncertainty around possible regional differences in aflatoxin contamination and the data set is likely not to be fully representative of food for the EU market. " The CONTAM Panel considers that this is sufficiently addressed in the opinion.
			It is also not possible to check the concentrations of food groups level 1 are dominated by one food level 3 or more foods of level 3. Summary lines 127-130: CONTAM writes "Overall, 'grains and grain-based products' made the largest contribution to the LB mean chronic dietary exposure to AFB1 in all age classes. The main subcategories driving the contribution of this food category were 'grains for human consumption' (in particular rice), 'bread and rolls' and 'fine bakery wares'", showing that the information is available.	The CONTAM Panel acknowledges the comment. E.5 bis (A) and E.7 bis (A) have been added to Annex E and present the contributing foods at the FoodEx level used for dietary exposure for AFB1 and AFT+M1.
			RIVM requests CONTAM to show in sheet B7 information on occurrence data of all aflatoxins per food group and foods (level 1, 2 and 3) and not only AFM1.	A filter was applied in Table B.7, due to which the data for the other aflatoxins were not shown. This has been corrected in the final version.
			table 8: The food group 'Animal and vegetable fats and oils' shows 4% positive concentration for AFM1 (n=26 samples). The group 'Animal and vegetable fats and oils' covers butter, thus AFM1 is expected for this group. Information in Annex table E6 shows that 'Animal and vegetable fats and oils' has not been included in the exposure assessment of AFM1. A reason for this is not discussed. Could CONTAM explain why the samples of 'Animal and vegetable fats and oils' were not included in the assessment?	The 26 samples consisted of 25 samples of butter (all left-censored) and 1 sample of butter oil (quantified concentration of AFM1). Considering the large influence of one positive sample on a broadly consumed food group, these samples were not included in the dietary exposure assessment. This information was added to Section 3.3.1.2.

Stakeholder	Comment number	Chapter	Comment	EFSA response
	64	3.3.1 Current dietary exposure assessment	Paragraph 3.3.1.2. Contributions of different food groups lines 2401-2462. The LB scenarios across all surveys clearly showed that the food group 'grains and grain-based products' was the dominant driver of the mean exposure. The annexes only provide information on contributions for the LB mean exposure. The contribution of LB 95th percentile contributions and UB mean/95th percentile contributions are not provided, nor discussed. RIVM requests CONTAM to add contribution of LB 95th and UB mean and P95th percentile contributions.	The CONTAM Panel acknowledges the comments and calculated the main contributors to the AFB1, AFM1 and AFT+AFM1 LB mean exposure for highly exposed individuals identified as subjects having an individual exposure level above the 75th percentile of the overall exposure calculated for the total population. The results are shown in Annex E, Table E.5 bis (B), Table E.6 (B) and Table E.7 bis (B).
	65	References	[References, lines 3154-3156] Note that the FAO/WHO evaluation of aflatoxins (83rd report of JECFA) is dated on 2018 in the draft opinion, while this FAO/WHO report is dated on 2017 (as correctly referred to in EFSA CONTAM 2018). We would suggest to correct this throughout the opinion.	In the current opinion, reference is made to the full monograph which was published in 2018. The correct reference is: FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2018. Aflatoxins. Safety evaluation of certain contaminants in food: prepared by the eighty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series, No 74; 2-280. The reference list has been updated accordingly.
	66	Annex A: Dietary surveys per country and age group available in the EFSA Comprehensive Database, considered in the exposure assessment	CONTAM provided underlying data information in 5 annexes (xlsx). All annexes are frozen and difficult to analyse, e.g. the filter options are blocked. RIVM suggests CONTAM to unlock the filter options. o Annex A: According to the description of Dutch survey DNFCS-Young-Children the number of food records (re-call days) is 3', but actually the number of re-call days is '2'. RIVM requests CONTAM to update number of re-call days for DNFCS-Young-Children with the value '2''	Thank you for this comment. EFSA will publish the unblocked annexes with the final opinion. Thank you for spotting this. The CONTAM Panel corrected it accordingly.
	67	Annex B: Occurrence	Annex B presents information on aflatoxin occurrence data. Not all sheets provide data on FoodEx level 3, only sheet table_B_7, and in this sheet only data on AFM1 can be viewed. RIVM proposes CONTAM to update Annex B	A filter was applied in Table B.7, due to which the data for the other aflatoxins were

Stakeholder	Comment number	Chapter	Comment	EFSA response
		data on aflatoxins	with occurrence data information on FoodEx level 3 (preferably even level 4) for all subtypes of aflatoxin.	not shown. This has been corrected in the final version.
	68	Annex E: Mean and high chronic dietary exposure to aflatoxins per survey and the contribution of different food groups to the dietary exposure	Annex E: presents information on dietary exposure to aflatoxins per survey and the contribution of different food groups to the dietary exposure. It would be interesting to review the relative contribution of food groups (level 2 or higher) to the total exposure per survey. RIVM proposes CONTAM to update Annex E with this information.	Thank you for this suggestion; The CONTAM Panel acknowledges the relevance of this information for the Member States. The CONTAM Panel will take this suggestion into consideration for future work. However, in the context of the current opinion and deadline this information cannot be provided.

Appendix 1: Explanatory note to Public Consultation

EFSA's Panel on Contaminants in the Food Chain (CONTAM) has launched an open consultation on the draft risk assessment of aflatoxins in food. This document presents estimations of human dietary exposure to aflatoxins and an assessment of human health risks related to dietary exposure to aflatoxins.

Interested parties are invited to submit written comments by 15 November 2019.

Please use the electronic template provided:

https://ec.europa.eu/eusurvey/runner/AFLATOXINSPC2019 to submit comments and refer to the line and page numbers. To submit additional data to support your comments or files, there is an upload function available in the tool (for a maximum size of 1Mb file).

Otherwise you can also contact specific unit's functional mailbox: biocontam@efsa.europa.eu

Please note that comments will not be considered if they:

- are submitted after the closing date of the consultation
- are presented in any form other than what is provided for in the instructions and template
- are not related to the contents of the document
- 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.

EFSA will assess all comments which are submitted in line with the criteria above. The comments will be further considered by the relevant EFSA Panel and taken into consideration if found to be relevant. Due to time constraints, EFSA cannot use additional occurrence data submitted during the public consultation for the dietary exposure assessment in this risk assessment. However, occurrence data submitted in SSD format will be stored and used for future risk assessments.

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Publication of contributions

Contributions will be published (as part of an EFSA report published together with the final opinion) and may be re-used by EFSA in a different context. It should be noted that contributions submitted by individuals in a personal capacity will be published as such, indicating the author's first and family name, unless a substantial justification for protection is provided by the respondent. Contributions submitted on behalf of an organisation are also made publicly available and attributed to the organization in question.

Submit comments (deadline: 17 September 2019)

Published:

4 October 2019

References

Bailey GS, Dashwood R, Loveland PM, Pereira C and Hendricks JD, 1998. Molecular dosimetry in fish: quantitative target organ DNA adduction and hepatocarcinogenicity for four aflatoxins by two exposure routes in rainbow trout. Mutation Research, 399:233-244.

CCCF (Codex Committee on Contaminants in Foods), 2018. Report of the 12th session of the Codex Committee on Contaminants in foods. FAO/WHO. Available online: http://www.fao.org/fao-who-codexalimentarius/committees/committee/en/?committee=CCCF

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2018. Effect on public health of a possible increase of the maximum level for 'aflatoxin total' from 4 to 10 mu g/kg in peanuts and processed products thereof, intended for direct human consumption or use as an ingredient in foodstuffs. EFSA Journal 2018; 16(2):5175, 32 pp. doi: 10.2903/j.efsa.2018.5175

EFSA (European Food Safety Authority), 2007a. Opinion of the scientific panel on contaminants in the food chain (CONTAM) related to the potential increase of consumer health risk by a possible increase of the existing maximum levels for aflatoxins in almonds, hazelnuts and pistachios and derived products. EFSA Journal 2007;5(3): 446, 127 pp.doi: 10.2903/j.efsa.2007.446

EFSA, 2005. Opinion of the Scientific Committee on a request from EFSA related to a harmonized approach for risk assessment of substances which are both genotoxic and carcinogenic. EFSA Journal, 3:e00282. doi: 10.2903/j.efsa.2005.282

European Commission, 2018a. European Union comments for the Codex Committee on Contaminants in Food 12th session. Proposed draft maximum level for total aflatoxins in ready-to-eat peanuts and associated sampling plan. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/codex_cccf_12_agenda_item_10.pdf

European Commission, 2018b. European Union comments for the Codex Committee on Contaminants in Food 12th session. Proposed draft maximum levels for total aflatoxins and ochratoxin A in nutmeg, chilli and paprika, ginger, pepper and turmeric and associated sampling plans. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/codex_cccf_12_agenda_item_11.pdf

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2018. Aflatoxins. Safety evaluation of certain contaminants in food: prepared by the eighty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series, No 74; 2-280.

Hasanzadeh S and Rezazadeh L, 2013. Effects of aflatoxin B1 on the growth processes of spermatogenic cell series in adult male rats. Comparative Clinical Pathology, 22:555-562.

McKean C, Tang L, Tang M, Billam M, Wang Z, Theodorakis CW, Kendall RJ and Wang JS, 2006a. Comparative acute and combinative toxicity of aflatoxin B1 and fumonisin B1 in animals and human cells. Food and Chemical Toxicology 44, 868-876.

McKean C, Tang L, Billam M, Tang M, Theodorakis CW, Kendall RJ and Wang JS, 2006b. Comparative acute and combinative toxicity of aflatoxin B1 and T-2 toxin in animals and immortalized human cell lines. J Appl Toxicol, 26, 139-147.

McMillan A, Renaud JB, Burgess KMN, Orimadegun AE, Akinyinka OO, Allen SJ, Miller JD, Reid G and Sumarah MW, 2018. Aflatoxin exposure in Nigerian children with severe acute malnutrition. Food and Chemical Toxicology, 111, 356-362.

Pottenger LH, Andrews LS, Bachman AN, Boogaard PJ, Cadet J, Embry MR, Farmer PB, Himmelstein MW, Jarabek AM, Martin EA, Mauthe RJ, Persaud R, Preston RJ, Schoeny R, Skare J, Swenberg JA, Williams GM, Zeiger E, Zhang F and Kim JH, 2014. An organizational approach for the assessment of DNA adduct data in risk assessment: case studies for aflatoxin B-1, tamoxifen and vinyl chloride. Critical Reviews in Toxicology, 44, 348-391.

WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 2009. Principles and Methods for the Risk Assessment of Chemicals in Food, International Programme on Chemical Safety, Environmental Health Criteria 240. Chapter 6: Dietary Exposure Assessment of Chemicals in Food. Available online: http://www.who.int/ipcs/food/principles/en/index1.html.

Wheeler M, 2019. Re: EFSA opinion on aflatoxins_use of restricted/unrestricted models. Message to Katleen Baert. 11 December 2019. E-mail.

Williams DE, 2012. The rainbow trout liver cancer model: response to environmental chemicals and studies on promotion and chemoprevention. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 155:121-127.

Williams DE, Orner G, Willard KD, Tilton S, Hendricks JD, Pereira C, Benninghoff AD and Bailey GS, 2009. Rainbow trout (*Oncorhynchus mykiss*) and ultra-low dose cancer studies. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 149C:175-181.

Wogan GN, Paglialunga S and Newberne PM, 1974. Carcinogenic effects of low dietary levels of aflatoxin B1 in rats. Food and Cosmetics Toxicology, 12:681-685. doi: https://doi.org/10.1016/0015-6264(74)90239-9

Abbreviations

AF-alb	Aflatoxin albumin adduct
AFB1	Aflatoxin B1
AFB1-lys	Aflatoxin B1 lysine adduct
AFB1-N7-gua	Aflatoxin B1-N7-guanine
AFB2	Aflatoxin B2
AFG1	Aflatoxin G1
AFG2	Aflatoxin G2
AFM1	Aflatoxin M1
AFM2	Aflatoxin M2
AFT	Aflatoxin total
ARfD	Acute reference dose
BMD	Benchmark dose
BMDL	Benchmark dose lower confidence limit
BMR	Benchmark response
bw	Body weight
CCCF	Codex Committee on Contaminants in Food
CONTAM	Panel on Contaminants in the Food Chain
EC	European Commission
EFSA	European Food Safety Authority
ELISA	enzyme linked immunosorbent assay
EU	European Union
FAO	Food and Agriculture Organization
HBGV	Health-based guidance value
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus

HPLC	High-performance liquid chromatography
HR	High resolution
IARC	International Agency for Research on Cancer
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LB	Lower bound
LC	Liquid chromatography
LCD	Left-censored data
LD_{50}	Lethal dose killing 50% of the animals
LOAEL	Lowest-observed-adverse-effect-level
LOD	Limit of detection
LOQ	Limit of quantification
ML	Maximum level
MOE	Margin of exposure
MS	Mass spectrometry
NOAEL	no-observed-adverse-effect-level
UB	Upper bound