CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 3(a) **CX/FA 23/53/3**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

Fifty-third Session

MATTERS OF INTEREST ARISING FROM FAO/WHO AND FROM THE 92ND AND 95TH MEETINGS OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA) RESPECTIVELY

Matters for information from FAO

1. The 171st Session of the FAO Council (December 2022) has endorsed the FAO Strategic Priorities for Food Safety[1]. The Strategic Priorities describe how FAO's work on food safety will contribute to the 2030 Agenda in alignment with FAO's Strategic Framework 2022-31. The Strategic Priorities for Food Safety are articulated around four Strategic Outcomes that result from an iterative consultative process led by FAO with its Members and international partner organizations. Those include strong multi-stakeholder governance for food safety, strong science to support food safety decisions, strong national food control systems and strong public-private cooperation for food safety. These Strategic Priorities encourage a more consistent integration of food safety in the development of sustainable and inclusive agrifood systems, food security and nutrition policies, and agriculture development strategies.

Matters for information from WHO

2. Non-sugar sweeteners have been developed as an alternative to sugars and are widely used both as an ingredient in pre-packaged foods and beverages and added to food and beverages directly by the consumer. Individual non-sugar sweeteners undergo toxicological assessment by the JECFA and other authoritative bodies to establish safe levels of intake (i.e., acceptable daily intake or ADI). While results of randomized controlled trials have generally suggested non-sugar sweeteners may have little impact on glucose metabolism and result in lower body weight when coupled with energy restriction in the short-term, there is no clear consensus on whether non-sugar sweeteners are effective for long-term weight loss or maintenance, or if they are linked to other long-term health effects at intakes within the ADI. In a report published by WHO in April 2022 based on a systematic review brings together the most current scientific evidence on health effects of non-sugar sweetener use[2].

3. The WHO Global Strategy for Food Safety 2022-2030 was adopted by the WHA75 in May 2022. It updates the last strategy in order to address current and emerging challenges, incorporate new technologies, and include innovative approaches for strengthening national food safety systems. This request was made by Member States in recognition that food safety remains a public health priority with a critical role in the achievement of the 2030 agenda for sustainable development. In developing this strategy WHO has had the support from the Technical Advisory Group on Food Safety: Safer Food for Better Health, consulted widely with scientific experts, with WHO regional advisors in food safety, international partners such as FAO and OIE, Member States and public consultation. Existing regional food safety action plans and food safety strategies were also taken into account, as well as the recommendations and guidelines of the Codex Alimentarius and the FAO food safety priorities. The WHO Global Strategy for Food Safety has been developed to guide and support Member States in their efforts to prioritize, plan, implement, monitor and regularly evaluate actions towards the reduction of the burden of foodborne diseases by continuously strengthening food safety systems and promoting global cooperation. WHO is now working to support Member States in the implementation of the strategy in collaboration with FAO, IFC-WB, TAG members and other partners. The implementation will be reported to WHA every two years until 2030.

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[1] FAO strategic priorities for food safety within the FAO Strategic Framework 2022-31: www.fao.org/3/nk093en/nk093en.pdf

[2] Health effects of the use of non-sugar sweeteners: a systematic review and meta-analysis, WHO 2022. https://www.who.int/publications/i/item/9789240046429

Matters for information from the 92nd and 95th meetings of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

4. The results of the 92nd meeting (Virtual meeting, 7-18 June 2021) and the 95th meeting (Virtual meeting, 6–17 and 22 June 2022) of JECFA on certain food additives are available as follows: the meeting report (WHO Technical Report Series 1037) and the toxicological and dietary exposure monographs (WHO Food Additive Series No 82 and No 83) are accessible through the WHO JECFA publications website: https://www.who.int/groups/joint-fao-who-expert-committee-on-food-additives-(jecfa)/publications#cms. The specification monographs resulting from the 92nd JECFA meeting are published as FAO JECFA Monographs 27, FAO, Rome, 2019. The publication is available on the FAO JECFA website at: http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-publications/en/. The specification monographs resulting from the 95th JECFA meeting will be published as FAO JECFA Monographs 30, FAO, Rome, 2022.

Requests for scientific advice

5. Both organizations continue to jointly prioritize the requests for scientific advice taking into consideration the criteria proposed by Codex as well as the requests for advice from Member Countries and the availability of resources. A list of all pending requests for scientific advice by JECFA will be posted on the respective FAO and WHO websites.

6. In scheduling the JECFA meetings and developing the agenda, the Joint Secretaries have to take into account the priorities requested by CCFA, CCCF, and CCRVDF. Due to the increasing requests for scientific advice to JECFA, not all requests can be addressed in the subsequent meeting. In prioritizing the work, the JECFA Secretariat takes into account existing criteria, on-going Codex work and available resources.

7. To facilitate provision of extra-budgetary resources for scientific advice activities, please contact Dr Markus Lipp, FAO Food Safety and Quality Unit (jecfa@fao.org) and Kim Petersen, Department of Nutrition and Food Safety, WHO (jecfa@who.int).

Actions required as a result of changes in acceptable daily intake (ADI) status and other toxicological recommendations from JECFA

8. At its 92nd meeting, JECFA evaluated the safety of two food additives (including one group of food additives) and four processing aids (Toxicological recommendations or other scientific advice for these food additives are provided in the attached Annex 1) and specifications for seven food additives (including new specifications and revised specification) were prepared (See CX/FA 23/53/4, Annex 1) . CCFA53 is invited to consider the recommended actions (presented in Annex 1 to this document) which might be required following the evaluations of these food additives.

9. At its 95th meeting, JECFA evaluated the safety of nine food processing aids, prepared specification for two food additives (including new specifications and revised specifications) and evaluated the safety of one group of flavoring agents (Toxicological recommendations or other scientific advice for these food additives are provided in the attached Annex 2)). JECFA also prepared specification for two food additives (including new specifications and revised specifications) and one group of flavouring agents (See CX/FA 23/53/4, Annex 1). CCFA53 is invited to consider the recommended actions (presented in Annex 2 to this document) which might be required following the evaluations of these food additives.

10. At its 95th meeting, JECFA reviewed the list of enzyme preparations for evaluation and noted that there were two different formats for the title. Reflecting on past evaluations and considering ease of use, JECFA decided that the name given to the enzyme preparation should correspond to the name of the enzyme activity or activities that most accurately characterize the preparation, the donor(s) of the genetic material and the production microorganism. However, at its 95th meeting, JECFA noted that by following this naming convention, two of the enzyme preparations would have the same name; the Committee therefore decided that an identification system would also be used for all enzyme preparations, consisting of the JECFA meeting number followed by the agenda item number of the substance (e.g., JECFA95-1).

11. Under the current JECFA enzymes guidelines described in Environmental Health Criteria 240, toxicological data and dietary exposure information are not required for Class 1, Type iii preparations. However, for many of the enzyme preparations that the JECFA considers, toxicological data and dietary exposure assessment data are available. At its 95th meeting, JECFA therefore wishes to emphasize that, when such data exist, they should be submitted to the JECFA for evaluation.

12. At its 95th meeting, JECFA discussed the requests for confidentiality made by sponsors for some information and determined that any information that can be found in the public domain will be included in JECFA publications as necessary.

13. At its 95th meeting, JECFA expressed its frustration that many of the current data submissions were inconsistent with key aspects of the guidelines published by the JECFA. At its 95th meeting, JECFA noted when preparing the specifications monographs for individual enzyme preparations that a considerable amount of supporting information was not made available, even when requested on more than one occasion. In addition, the details of the assays supplied included the use of an enzyme reference or calibrant, rather than a direct link to an original enzyme assay from which a meaningful unit definition could be derived. The consequence of the absence of such data has resulted in JECFA at its 95th meeting designating many of the enzyme specifications "tentative" and toxicological evaluations "temporary" at the present meeting. It should also be noted that, for one enzyme preparation, JECFA became aware that highly relevant toxicological studies, now known to have been submitted to at least one regulatory body in 2005, were not submitted to JECFA. At its 95th meeting, JECFA asks the joint FAO/WHO JECFA Secretariat to urge sponsors and Codex Members to ensure that all required information is available for evaluation prior to requesting inclusion in the Codex Committee on Food Additives JECFA Priority List.

Annex 1

Food additives evaluated toxicologically and/or considered for specifications at the 92nd JECFA meeting

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
210 211 212 213	Benzoic acid, its salts and derivatives	The 92nd JECFA evaluated a new extended one-generation reproductive toxicity study on benzoic acid. This study showed no treatment-related adverse effects, indicating a NOAEL of 1000 mg/kg bw per day, the highest dose tested. Applying a chemical specific adjustment factor of 2 for interspecies toxicokinetics variation instead of the default factor of 4.0, **the 92nd JECFA established a group ADI of 0–20 mg/kg bw**, which applies to benzoic acid, the benzoate salts (calcium, potassium and sodium), benzaldehyde, benzyl acetate, benzyl alcohol and benzyl benzoate, expressed as benzoic acid equivalents. **The 92nd JECFA withdrew the previous group ADI of 0–5 mg/kg bw.** The 92nd JECFA noted that the high dietary exposure estimate, expressed as benzoic acid, of 7.1 mg/kg bw per day for children aged 3–9 years does not exceed the group ADI of 0–20 mg/kg bw.	Note the JECFA conclusion that the new data that have become available since the previous evaluation of benzoic acid, its salts and derivatives give reason to revise the ADI. Note that JECFA withdrew the previous group ADI of 0–5 mg/kg bw benzoic acid, its salts and derivatives and established a new group ADI of 0–20 mg/kg bw. The new group ADI applies to benzoic acid, the benzoate salts (calcium, potassium and sodium), benzaldehyde, benzyl acetate, benzyl alcohol and benzyl benzoate, expressed as benzoic acid equivalents. Note the new specifications for benzoic acid, its salts and derivatives (see CX/FA 23/53/4).
	Collagenase from *Streptomyces violaceoruber* expressed in *S. violaceoruber*	Negative results were observed in genotoxicity studies with a powdered enzyme concentrate. The 92nd JECFA identified a NOAEL of 940 mg TOS/kg bw per day (rounded from 939.6), the highest dose tested in a 13-week study of oral toxicity in rats. The 92nd JECFA identified a NOAEL of 940 mg TOS/kg bw per day, the highest dose tested in a 13-week study of oral toxicity in rats. Comparison of this NOAEL with the estimated dietary exposure of 0.43 mg TOS/kg bw per day gave a margin of exposure (MOE) of > 2100. In view of this MOE and the lack of concern about genotoxicity, the **92nd JECFA established an ADI "*not specified*"[3] for collagenase from *S. violaceoruber*,** when used in the applications	Note that JECFA established an ADI "*not specified*" for collagenase from *S. violaceoruber*, when used in the applications specified and in accordance with good manufacturing practice. Note the new JECFA specifications for collagenase from *Streptomyces violaceoruber*

[3] The reader is referred to the Technical Report of the 87th JECFA meeting for clarification of the term "*ADI not specified*".

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		specified and in accordance with good manufacturing practice.	expressed in *S. violaceoruber* (see CX/FA 23/53/4).
	β-Glucanase from *Streptomyces violaceoruber* expressed in *S. violaceoruber*	The 92nd JECFA noted negative results in studies of genotoxicity and in studies of oral toxicity in rats. The 92nd JECFA identified a NOAEL of 950 mg TOS/kg bw per day (rounded by the 92nd JECFA from 953.3), the highest dose tested. Comparison of this NOAEL with the estimated dietary exposure of 0.15 mg TOS/kg bw per day gave an MOE >6300. On the basis of this MOE and the lack of concern about genotoxicity, the 92nd **JECFA established an ADI "*not specified*"[3] for β-glucanase from *S. violaceoruber*,** for the proposed uses and in accordance with good manufacturing practice.	Note that JECFA established an ADI "*not specified*" for β-glucanase from *S. violaceoruber* for the proposed uses and in accordance with good manufacturing practice. Note the new JECFA specifications for β-Glucanase from *Streptomyces violaceoruber* expressed in *S. violaceoruber* (see CX/FA 23/53/4).
	Phospholipase A2 from *Streptomyces violaceoruber* expressed in *S. violaceoruber*	The 92nd JECFA noted negative results were obtained in genotoxicity tests. In a 13-week study of oral toxicity in rats, small effects were seen at low incidence at the high dose of 956 mg TOS/kg bw per day, which might have been related to treatment. The 92nd JECFA therefore identified a NOAEL of 190 mg TOS/kg per day (rounded by the 92nd JECFA from 191 mg TOS/kg bw per day). A comparison of the estimated dietary exposure of 0.25 mg TOS/kg bw per day with the NOAEL of 190 mg TOS/kg bw per day from the oral toxicity study gives a MOE of 760. On this basis and in the absence of concern about genotoxicity, the 92nd **JECFA established an ADI "*not specified*"[3] for the phospholipase A2 enzyme preparation from *S. violaceoruber*** when used in the applications specified and in accordance with good manufacturing practice.	Note that JECFA established an ADI "*not specified*" for the phospholipase A2 enzyme preparation from *S. violaceoruber* when used in the applications specified and in accordance with good manufacturing practice. Note the existing specifications for phospholipase A2 enzyme preparation from *Streptomyces violaceoruber expressed in S. violaceoruber* were revised (see CX/FA 23/53/4).
101(iv)	Riboflavin from *Ashbya gossypii*	The 92nd JECFA noted that riboflavin from *A. gossypii* has low acute toxicity and does not raise concern for genotoxicity. The NOAEL from a 90-day oral toxicity study in rats was 3000 mg/kg bw per day, the highest dose tested. Comparison of this NOAEL with the estimated dietary exposure of 3.6 mg/kg bw per day, based on maximum reported use levels, resulted in an MOE > 800. **The 92nd JECFA established a group ADI "*not specified*"[3] for riboflavin, riboflavin- 5´-phosphate, riboflavin from *B. subtilis* and riboflavin from *A. gossypii*, expressed as riboflavin**.	Note that JECFA established a group ADI "*not specified*" for riboflavin, riboflavin-5´-phosphate, riboflavin from *B. subtilis* and riboflavin from *A. gossypii*, expressed as riboflavin. Note that JECFA withdrew the previous

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		The 92nd JECFA withdrew the previous group ADI of 0–0.5 mg/kg bw. The 92nd JECFA noted that in view of information received implies that riboflavin is no longer produced synthetically for use as a food additive, the 92nd JECFA recommends that the CCFA reconsider the requirement for specifications for synthetically produced riboflavin. The 92nd JECFA noted that for future work that the previously established specifications for riboflavin and riboflavin from *B. subtilis*, JECFA proposes to: • Rename "riboflavin" as "riboflavin, synthetic"; • Replace the existing method for determination of lumiflavin in both specifications to avoid use of chloroform; and • Delete the functional use of "nutrient supplement" from the specifications monograph on riboflavin from B. subtilis, as the Codex food additive definition does not include nutrients.	group ADI of 0–0.5 mg/kg bw. Note the new JECFA specifications for Riboflavin from *Ashbya gossypii* (see CX/FA 23/53/4). Note that JECFA remarked that riboflavin is no longer produced synthetically for use as a food additive and recommends that the CCFA reconsider the requirement for specifications for Riboflavin, synthetic (INS 101(i)).
	Ribonuclease P from *Penicillium citrinum*	The 92nd JECFA identified a NOAEL of 980 mg TOS/kg bw per day (the highest dose tested) in a 13-week study in which rats were treated with ribonuclease P concentrate from *P. citrinum* AE-RP by gavage. A comparison of the estimated dietary exposure of 1.3 mg TOS/kg bw per day with the NOAEL of 980 mg TOS/kg bw per day gives an MOE > 750. On the basis of this MOE and the lack of concern for genotoxicity, **the 92nd JECFA established an ADI "*not specified*" [3] for the ribonuclease P enzyme preparation from *P. citrinum* AE-RP**, used in the applications specified and in accordance with good manufacturing practice. The 92nd JECFA noted that ribonuclease P can also be produced by *P. citrinum* RP-4, but insufficient information was available on the enzyme concentrate produced from this strain. To evaluate the safety of ribonuclease P from *P. citrinum* RP-4, toxicological studies with well-characterized enzyme concentrate are required.	Note that JECFA established an ADI "*not specified*" for the ribonuclease P enzyme preparation from *P. citrinum* AE-RP, used in the applications specified and in accordance with good manufacturing practice. Note the new JECFA specifications for the ribonuclease P from *P. citrinum* AE-RP (see CX/FA 23/53/4).

Annex 2

Food additives evaluated toxicologically and/or considered for specifications at the 95th JECFA meeting

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
	α-Amylase from *Geobacillus stearothermophilus* expressed in *Bacillus licheniformis*	The 95th JECFA concluded that dietary exposure to this α-amylase is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 67 mg TOS/kg bw per day, the highest dose tested in a 13-week oral toxicity study in rats. When this NOAEL is compared with the dietary exposure estimate of 0.2 mg TOS/kg bw per day, a MOE of more than 330 can be calculated. Based on this MOE and the lack of concern for genotoxicity, **the 95th JECFA established a temporary ADI "*not specified*"[4] for α-amylase (JECFA95-1) from *G. stearothermophilus* expressed in *B. licheniformis***, when used in the applications specified, at the levels of use specified and in accordance with current GMP. This ADI "*not specified*" was made temporary because of the tentative nature of the specifications. The 95th JECFA requested the following information, by the end of 2023, to complete the safety assessment: • validated method of analysis to determine α-amylase activity, including the validation report; • unit definition for α-amylase activity based on the method of assay; and • analytical data using the validated method for at least five different batches of commercially available products.	Note that JECFA established a temporary ADI "*not specified*" for α-amylase from *G. stearothermophilus* expressed in *B. licheniformis*, when used in the applications specified, at the levels of use specified and in accordance with current GMP. This ADI was made temporary because of the tentative nature of the specifications. Note the new tentative specifications for α-Amylase from *Geobacillus stearothermophilus* expressed in *Bacillus licheniformis* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.
	α-Amylase from *Geobacillus stearothermophilus* expressed in *Bacillus licheniformis*	The 95th JECFA concluded that dietary exposure to this α-amylase is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 660mg TOS/kg bw per day, the highest dose tested in a 13-week oral toxicity study in rats. When this NOAEL is compared with the dietary exposure estimate of 0.08mg TOS/kg bw per day, a MOE of more than 8000 can be calculated. Based on this MOE and the lack of concern for genotoxicity, the 95th JECFA established a temporary ADI "*not specified*" for α-amylase (JECFA95-2) from *G. stearothermophilus* expressed in *B.*	Note that JECFA established a temporary ADI "*not specified*" for α-amylase (JECFA95-2) from *G. stearothermophilus* expressed in *B. licheniformis*, when used in the applications specified, at the levels of use specified and in accordance with current GMP. This ADI was made temporary because of

[4] The reader is referred to the Technical Report of the 87th JECFA meeting for clarification of the term "*ADI not specified*".

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		licheniformis, when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI "*not specified*" was made temporary because of the tentative nature of the specifications. The 95th JECFA requested the following information, by the end of 2023, to complete the safety assessment: • validated method of analysis to determine α-amylase activity, including the validation report; • unit definition for α-amylase activity based on the method of assay; and • analytical data using the validated method for at least five different batches of commercially available products.	the tentative nature of the specifications. Note the new tentative specifications for α-Amylase from *Geobacillus stearothermophilus* expressed in *Bacillus licheniformis* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.
	α-Amylase from *Rhizomucor pusillus* expressed in *Aspergillus niger*	The 95th JECFA concluded that dietary exposure to this α-amylase is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 1400 mg TOS/kg bw per day, the highest dose tested in a 13-week oral toxicity study in rats. When this NOAEL is compared with the dietary exposure estimate of 4 mg TOS/kg bw per day, a MOE of more than 350 can be calculated. Based on this MOE and the lack of concern for genotoxicity, **the 95th JECFA established a temporary ADI "*not specified*"[4] for α-amylase (JECFA95-3) from *R. pusillus* expressed in *A. niger***, when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI "*not specified*" was made temporary because of the tentative nature of the specifications. The 95th JECFA requested the following information, by the end of 2023, to complete the safety assessment: • validated method of analysis to determine α-amylase activity, including the validation report; • unit definition for α-amylase activity based on the method of assay; and • analytical data using the validated method for at least five different batches of commercially available products.	Note that JECFA established a temporary ADI "*not specified*" for α-amylase (JECFA95-3) from *R. pusillus* expressed in *A. niger*, when used in the applications specified, at the levels of use specified and in accordance with current GMP. This ADI was made temporary because of the tentative nature of the specifications. Note the new tentative specifications for α-Amylase from *Rhizomucor pusillus* expressed in *Aspergillus niger* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
	Amyloglucosidase from *Rasamsonia emersonii* expressed in *Aspergillus niger*	The 95th JECFA noted that amyloglucosidase may pose a risk as a respiratory allergen. In the absence of any information regarding its stability within the gastrointestinal tract, the 95th JECFA could not complete the assessment of the risk for allergenicity from dietary exposure to this enzyme. The 95th JECFA identified a NOAEL of 1500 mg TOS/kg bw per day in a 13-week study of oral toxicity in rats. When this NOAEL, the highest dose tested, is compared with the conservative dietary exposure estimate of 9 mg TOS/kg bw per day, a MOE of more than 160 can be calculated. Based on this MOE and the lack of concern for genotoxicity, the **95th JECFA established a temporary ADI "*not specified*" [4] for amyloglucosidase (JECFA95-4) from *R. emersonii* expressed in *A. niger*** when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI "*not specified"* was made temporary because of the tentative nature of the specifications and the inability to complete the allergenicity assessment. The 95th JECFA requested the following information, by the end of 2023, to complete the safety assessment: • digestibility data in order to complete the allergenicity assessment; • validated method of analysis to determine amyloglucosidase activity, including the validation report; • unit definition for amyloglucosidase activity based on the method of assay; and • analytical data using the validated method for at least five different batches of commercially available products.	Note that JECFA established a temporary ADI "*not specified*" for amyloglucosidase (JECFA95-4) from *R. emersonii* expressed in *A. niger* when used in the applications specified, at the levels of use specified and in accordance with current GMP. Note the new tentative specifications for *R* Amyloglucosidase from *Rasamsonia emersonii* expressed in *Aspergillus niger* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.
	Asparaginase from *Pyrococcus furiosus* expressed in *Bacillus subtilis*	The 95th JECFA concluded that dietary exposure to the enzyme preparation is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 1207 mg TOS/kg bw per day, the highest dose tested, in a 13-week study of oral toxicity in rats. When this NOAEL is compared with dietary exposure estimate of 0.4 mg TOS/kg bw per day, a MOE of more than 3000 can be calculated. Based on this MOE and the lack of concern for genotoxicity, **the 95th JECFA**	Note that JECFA established a temporary ADI "*not specified*" for asparaginase (JECFA95-5) from *P. furiosus* expressed in *B. subtilis* when used in the applications specified, at the levels of use specified and in accordance with current GMP.

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		established a temporary ADI "*not specified*"[4] for asparaginase (JECFA95-5) from *P. furiosus* expressed in *B. subtilis* when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI "*not specified*" was made temporary because of the tentative nature of the specifications. The 95th JECFA requested the following information, by the end of 2023, to complete the safety assessment: • validated method of analysis to determine asparaginase activity, including the validation report; • unit definition for α-amylase activity based on the method of assay; and • analytical data using the validated method for at least five different batches of commercially available products.	This ADI was made temporary because of the tentative nature of the specifications. Note the new tentative specifications for Asparaginase from *Pyrococcus furiosus* expressed in *Bacillus subtilis* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.
	β-Amylase from *Bacillus flexus* expressed in *Bacillus licheniformis*	The 95th JECFA concluded that dietary exposure to the enzyme preparation is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 1199 mg TOS/kg bw per day, the highest dose tested, in a 13-week study of oral toxicity in rats. When this NOAEL is compared with the dietary exposure estimate of 1mg TOS/kg bw per day, a MOE of around 1200 can be calculated. Based on this MOE and the lack of concern for genotoxicity, **the 95th JECFA established a temporary ADI "*not specified*"[4] for β-amylase (JECFA95-6) from *B. flexus* expressed in *B. licheniformis*** when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI "not specified" was made temporary because of the tentative nature of the specifications.	Note that JECFA established a temporary ADI "*not specified*" for β-amylase from *B. flexus* expressed in *B. licheniformis* when used in the applications specified, at the levels of use specified and in accordance with current GMP. This ADI was made temporary because of the tentative nature of the specifications. Note the new tentative specifications for β-amylase from *B. flexus* expressed in *B. licheniformis* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
	Lipase from *Thermomyces lanuginosus* and *Fusarium oxysporum* expressed in *Aspergillus oryzae*	The 95th JECFA concluded that dietary exposure to this lipase is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 1080 mg TOS/kg bw per day, the highest dose tested in the 13-week study of oral toxicity in rats. When this NOAEL is compared with the dietary exposure estimate of 0.2 mg TOS/kg bw per day, a MOE of more than 5000 can be calculated. Based on this MOE and the lack of concern for genotoxicity, the **95th JECFA established an ADI "*not specified*" [4] for lipase (JECFA95-7) from *T. lanuginosus* and *F. oxysporum* expressed in *A. oryzae*** when used in the applications specified, at the levels of use specified and in accordance with current GMP.	Note that JECFA established an ADI "*not specified*" for lipase from *T. lanuginosus* and *F. oxysporum* expressed in *A. oryzae* when used in the applications specified, at the levels of use specified and in accordance with current GMP. Note the new specifications for Lipase from *Thermomyces lanuginosus* and *Fusarium oxysporum* expressed in *Aspergillus oryzae* (see CX/FA 23/53/4).
	Phospholipase A2 (PLA2) from porcine pancreas expressed in *Aspergillus niger*	**Because of the late submission of highly relevant toxicological data, other missing information and time constraints, the 95th JECFA was unable to complete this evaluation.** The 95th JECFA recommended that the evaluation of this enzyme preparation is completed at a future meeting. **The 95th JECFA requested the JECFA Secretariat to urge the sponsor and Codex Members to ensure that the following additional information is available for evaluation prior to requesting inclusion of this enzyme preparation in the CCFA JECFA Priority List:** • additional data to clarify the genotoxic potential of the PLA2 enzyme concentrate; • digestibility data for enzyme preparations containing both glucoamylase and PLA2; • results from five different batches of all types of PLA2 enzyme preparations using the assay to determine PLA2 activity provided in the dossier; • validation information of the alternative method of analysis used to determine PLA2 activity (this should include the method description in English); • unit definition for the PLA2 activity based on the alternative method of assay; and	Note that JECFA was unable to complete the evaluation due to late submission of relevant data. Note the JECFA request for the JECFA Secretariat to urge the sponsor and Codex Members to ensure that the additional data requested by JECFA is available for evaluation prior to requesting inclusion of this enzyme preparation in the CCFA JECFA Priority List.

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		• analytical data using the alternative validated method for at least five different batches of all commercially available products.	
	Xylanase from *Bacillus licheniformis* expressed in *Bacillus licheniformis*	The 95th JECFA concluded that dietary exposure to this xylanase is not anticipated to pose a risk for allergenicity. The 95th JECFA identified a NOAEL of 1020mg TOS/kg bw per day, the highest dose tested, in the 13-week study of oral toxicity in rats. When this NOAEL is compared with the dietary exposure estimate of 0.01mg TOS/kg bw per day, a MOE of more than 100000 can be calculated. Based on this MOE and the lack of concern for genotoxicity, the 95th JECFA allocated a temporary ADI "*not specified"* for xylanase (JECFA95-9) from *B. licheniformis* expressed in *B. licheniformis* when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI "*not specified"* was made temporary because of the tentative nature of the specifications. The 95th JECFA requested the following information, by the end of 2023, to complete the safety assessment: • validated method of analysis to determine xylanase activity, including the validation report; • unit definition for α-amylase activity based on the method of assay; and • analytical data using the validated method for at least five different batches of commercially available products.	Note that JECFA established a temporary ADI "*not specified* for xylanase (JECFA95-9) from *B. licheniformis* expressed in *B. licheniformis* when used in the applications specified, at the levels of use specified and in accordance with current GMP. The ADI was made temporary because of the tentative nature of the specifications. This ADI was made temporary because of the tentative nature of the specifications. Note the new tentative specifications for Xylanase from *Bacillus licheniformis* expressed in *Bacillus licheniformis* (see CX/FA 23/53/4). Note the JECFA request for technical information by the end of 2023, to complete the safety assessment.

Flavouring agents evaluated at the 95th JECFA meeting

The flavouring agents were evaluated by the revised Procedure for the Safety Evaluation of Flavouring Agents.

Alicyclic ketones, secondary alcohols and related esters

Flavouring agent[5]	**No.**	**Specifications**	**Conclusion based on current estimated dietary exposure**
Trans-4-*tert*-butylcyclohexanol	2263	N	No safety concern
Caryophylla-3(4),8-dien-5-ol	2264	N	No safety concern

[5] Both flavouring agents are in structural class I.