

Appendix II

ACTION REQUIRED AS A RESULT OF CHANGES IN THE ACCEPTABLE DAILY INTAKE (ADI) STATUS
AND OTHER RECOMMENDATIONS ARISING FROM THE 99TH JECFA

(For information and action)

Food additives evaluated toxicologically and/or considered for specifications at the 99TH JECFA meeting

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommendation of CCFA55
	Adenosine-5 ϕ -monophosphate deaminase from <i>Aspergillus sp</i> (JECFA99-1)	The 99 th JECFA concluded that due to the lack of information to confirm the identity of the production organism and whether the test material used in the toxicity studies is representative of the current article of commerce, JECFA could not complete the safety evaluation of this enzyme preparation.	Note that JECFA could not complete the safety evaluation of this enzyme preparation.
163(xi)	Butterfly pea flower extract	Because of the limited nature of the toxicological data and the uncertainties concerning the specifications for the commercial product and the characterization of the test materials in the submitted toxicity studies, the 99 th JECFA was unable to complete the safety assessment of butterfly pea flower extract.	Note that JECFA could not complete the safety evaluation of Butterfly pea flower extract.
	Endo-1,4- β xylanase from <i>Bacillus subtilis</i> expressed in <i>Bacillus subtilis</i> (JECFA99-2)	The 99th JECFA concluded that dietary exposure to this endo-1,4-β-xylanase enzyme preparation is not anticipated to pose a risk for allergenicity. JECFA identified a NOAEL of 147.3 mg TOS/kg bw per day, the highest dose tested, in a 13-week study in rats. Comparison of this NOAEL with the estimated dietary exposure of 0.008 mg TOS/kg bw per day gives an MOE of more than 18 000. Based on this MOE and the lack of concern for genotoxicity, the 99th JECFA established an ADI “not specified” for endo-1,4-β-xylanase (JECFA99-2) from <i>Bacillus subtilis</i> expressed in <i>Bacillus subtilis</i> 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 endo-1,4-β-xylanase from <i>Bacillus subtilis</i> expressed in <i>Bacillus subtilis</i> when used in the applications specified, at the levels of use specified and in accordance with current GMP. Note the new specifications for endo-1,4-β-xylanase from <i>Bacillus subtilis</i> expressed in <i>Bacillus subtilis</i> (see CX/FA 25/54/4).
	Endo-1,4- β xylanase from <i>Rasamsonia emersonii</i> expressed in <i>Aspergillus niger</i> (JECFA99-3)	The 99th JECFA concluded that the risk of allergenicity upon dietary exposure to this endo-1,4-β-xylanase is low. JECFA identified a NOAEL of 1850 mg TOS/kg bw per day, the highest dose tested in the 13-week study in rats. Comparison of this NOAEL with the highest estimated dietary exposure of 0.380 mg TOS/kg bw per day in toddlers gave a margin of exposure (MOE) of more than 4800. Based on this MOE and lack of concern about genotoxicity, JECFA established an ADI “not specified” for this endo-1,4-β-xylanase (JECFA99-3) from <i>R. emersonii</i> expressed in <i>A. niger</i> when used in the applications	Note that JECFA established an ADI “ not specified ” for endo-1,4- β -xylanase from <i>Rasamsonia emersonii</i> expressed in <i>Aspergillus niger</i> when used in the applications specified, at the levels of use specified and in accordance with current GMP.

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		specified, at the levels of use specified and in accordance with GMP.	Note the new specifications for endo-1,4- β -xylanase from <i>Rasamsonia emersonii</i> expressed in <i>Aspergillus niger</i> (see CX/FA 25/54/4).
	Glucosidase from <i>Aspergillus niger</i> expressed in <i>Trichoderma reesei</i> exhibiting α -glucosidase and transglucosidase activity (JECFA99-4a, JECFA99-4b)	The 99th JECFA concluded that dietary exposure to this glucosidase is not anticipated to pose a risk for allergenicity. JECFA also had no concerns about potential genotoxicity of the enzyme concentrate. The Committee identified a NOAEL of 74.8 mg TOS/kg bw per day, the highest dose tested, for the enzyme concentrate in the 18-week study in rats. Comparison of this NOAEL with the estimated dietary exposure of 0.443 mg TOS/kg bw per day gave an MOE of 169. JECFA therefore established an ADI “<i>not specified</i>” for glucosidase from <i>A. niger</i> expressed in <i>T. reesei</i> exhibiting α-glucosidase (JECFA99-4a) and transglucosidase (JECFA99-4b) activity when used in the applications specified, at the levels of use specified and in accordance with GMP.	Note that JECFA established ADI “not specified” for glucosidase from <i>A. niger</i> expressed in <i>T. reesei</i> exhibiting α-glucosidase (JECFA99-4a) and transglucosidase (JECFA99-4b) activity when used in the applications specified, at the levels of use specified and in accordance with GMP. Note the new specifications for glucosidase from <i>A. niger</i> expressed in <i>T. reesei</i> exhibiting α-glucosidase (JECFA99-4a) and transglucosidase (JECFA99-4b) (see CX/FA 25/54/4).
235	Natamycin	The 99th JECFA concluded based on the available data, that there is no concern for the induction of antimicrobial resistance and that the risk of natamycin having a disrupting effect on the microbiome of the human gastrointestinal tract is low. JECFA re-affirmed the ADI of 0–0.3 mg/kg bw for natamycin established by the 20th JECFA. JECFA further noted that the NOAELs in the new 13-week and 1-year studies in rats (42 and 26 mg/kg bw per day, respectively), with the application of a 100-fold uncertainty factor, support the current ADI of 0–0.3 mg/kg bw.	Note that JECFA re-affirmed the ADI of 0–0.3 mg/kg bw for natamycin established by 20th JECFA. Note the revised specifications for natamycin (see CX/FA 25/54/4).
234 ¹	Nisin A	The 99th JECFA concluded based on the available data, that there is no concern for the induction of antimicrobial resistance, and that the risk of nisin having a disrupting effect on the microbiome of the human gastrointestinal tract is low. The new toxicological information available for this evaluation did not provide any reason to revise the ADI for nisin. JECFA re-affirmed the ADI of 0–2 mg/kg bw for nisin established by established by the 77th JECFA, but noted	Note that JECFA re-affirmed the ADI of 0–2 mg/kg bw for nisin A established by 77th JECFA. Note the revised specifications for nisin A (see CX/FA 25/54/4).

¹ According to the *Class Names and the International Numbering System for Food Additives* (CXG 36-1989), INS 234 is assigned to nisin and no INS number is designated for nisin A.

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		that the critical toxicological studies were conducted with nisin A; JECFA therefore concluded that the ADI applies only to nisin A.	
475	Polyglycerol esters of fatty acids	The 99th JECFA noted that at its 17th meeting, JECFA had established an ADI of 0–25 mg/kg bw for polyglycerol esters of fatty acids, based on a long-term study in rats in which there were no effects at 2500 mg/kg bw, the highest dose tested. In the absence of any new toxicological information, the 99th JECFA re-affirmed the ADI of 0–25 mg/kg bw for polyglycerol esters of fatty acids.	Note that JECFA re-affirmed the ADI of 0–25 mg/kg bw for polyglycerol esters of fatty acids established by established by the 17th JECFA. Considering the potential high exceedance of the ADI based on the estimated dietary exposures, CCFA should review and revise current uses of polyglycerol esters of fatty acids in the GSFA, including the maximum permitted levels and the food categories in which this food additive is permitted to be used. Note the revised specifications for polyglycerol esters of fatty acids (see CX/FA 25/54/4).