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SCIENTIFIC OPINION

Safety evaluation of the food enzyme rennet containing chymosin and pepsin A from the abomasum of suckling calves, goats, lambs and buffaloes

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Abstract

The food enzyme containing chymosin (EC 3.4.23.4) and pepsin (EC 3.4.23.1) is prepared from the abomasum of suckling calves, goats, lambs and buffaloes by Caglificio Clerici S.p.A. It is intended to be used in the production of cheese. As no concerns arise from the source of the food enzyme, from its manufacture and based on the history of safe use and consumption, the Panel considered that toxicological data were not required and no exposure assessment was necessary. The similarity of the amino acid sequences of the two proteins (chymosin and pepsin A) to those of known allergens was searched and two matches were found with respiratory allergens. The Panel considered that the risk of allergic reactions by dietary exposure cannot be excluded, but the likelihood is low. Based on the data provided, the Panel concluded that this food enzyme does not give rise to safety concerns under the intended conditions of use.

KEYWORDS

abomasum, buffaloes, chymosin, EC 3.4.23.1, EC 3.4.23.4, food enzyme, goats, lambs, pepsin, rennet, suckling calves

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1 | INTRODUCTION

Article 3 of the Regulation (EC) No 1332/2008[1] provides definition for 'food enzyme' and 'food enzyme preparation'.

'Food enzyme' means a product obtained from plants, animals or micro-organisms or products thereof including a product obtained by a fermentation process using micro-organisms: (i) containing one or more enzymes capable of catalysing a specific biochemical reaction; and (ii) added to food for a technological purpose at any stage of the manufacturing, processing, preparation, treatment, packaging, transport or storage of foods.

'Food enzyme preparation' means a formulation consisting of one or more food enzymes in which substances such as food additives and/or other food ingredients are incorporated to facilitate their storage, sale, standardisation, dilution or dissolution.

Before January 2009, food enzymes other than those used as food additives were not regulated or were regulated as processing aids under the legislation of the Member States. On 20 January 2009, Regulation (EC) No 1332/2008 on food enzymes came into force. This Regulation applies to enzymes that are added to food to perform a technological function in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food, including enzymes used as processing aids. Regulation (EC) No 1331/2008[2] established the European Union (EU) procedures for the safety assessment and the authorisation procedure of food additives, food enzymes and food flavourings. The use of a food enzyme shall be authorised only if it is demonstrated that:

- it does not pose a safety concern to the health of the consumer at the level of use proposed;
- there is a reasonable technological need;
- its use does not mislead the consumer.

All food enzymes currently on the European Union market and intended to remain on that market, as well as all new food enzymes, shall be subjected to a safety evaluation by the European Food Safety Authority (EFSA) and approval via an EU Community list.

The 'Guidance on submission of a dossier on food enzymes for safety evaluation' (EFSA, 2009a) lays down the administrative, technical and toxicological data required.

1.1 | Background and Terms of Reference as provided by the requestor

1.1.1 | Background as provided by the European Commission

Only food enzymes included in the European Union (EU) Community list may be placed on the market as such and used in foods, in accordance with the specifications and conditions of use provided for in Article 7(2) of Regulation (EC) No 1332/2008[1] on food enzymes.

Six applications have been introduced by the companies "Decernis, LLC", "Keller and Heckman LLP", the "Association of Manufacturers and Formulators of Enzyme Products (AMFEP)" and "Novozymes A/S" for the authorisation of the food enzymes Cyclomaltodextrin glucanotransferase from *Geobacillus stearothermophilus*, Dextranase from *Chaetomium gracile*, Subtilisin from *Bacillus licheniformis*, Mucorpepsin from *Rhizomucor miehei*, Animal rennet consisting of chymosin and pepsin from the abomasum of *Bos primigenius* (cattle), *Bubalus bubalis* (buffalo), *Capra aegagrus hircus* (goat) and *Ovis aries* (sheep), and Lipase from a genetically modified strain of *Aspergillus niger* (strain NZYM-DB), respectively.

Following the requirements of Article 12.1 of Regulation (EC) No 234/2011[3] implementing Regulation (EC) No 1331/2008,[2] the Commission has verified that the six application falls within the scope of the food enzyme Regulation and contains all the elements required under Chapter II of that Regulation.

1.1.2 | Terms of Reference

The European Commission requests the European Food Safety Authority to carry out the safety assessments on the food enzymes Cyclomaltodextrin glucanotransferase from *Geobacillus stearothermophilus*, Dextranase from *Chaetomium gracile*, Subtilisin from *Bacillus licheniformis*, Mucorpepsin from *Rhizomucor miehei*, Animal rennet consisting of chymosin and pepsin from the abomasum of *Bos taurus* (cattle), *Bubalus bubalis* (buffaloes), *Capra aegagrus hircus* (goat) and *Ovis aries* (sheep), and Lipase from a genetically modified strain of *Aspergillus niger* (strain NZYM-DB) in accordance with Article 17.3 of Regulation (EC) No 1332/2008 on food enzymes.

[1]Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on Food Enzymes and Amending Council Directive 83/417/EEC, Council Regulation (EC) No 1493/1999, Directive 2000/13/EC, Council Directive 2001/112/EC and Regulation (EC) No 258/97. OJ L 354, 31.12.2008, pp. 7–15.

[2]Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 354, 31.12.2008, pp. 1–6.

[3]Commission Regulation (EU) No 234/2011 of 10 March 2011 implementing Regulation (EC) No 1331/2008 of the European Parliament and of the Council establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 64, 11.3.2011, p. 15–24.

1.2 | Interpretation of the Terms of Reference

The present scientific opinion addresses the European Commission's request to carry out the safety assessment of food enzyme animal rennet consisting of chymosin and pepsin A from the abomasum of calves, young goats, lambs and buffaloes.

The application was submitted initially as a joint dossier[4] and identified as the EFSA-Q-2015-00237. During a meeting between EFSA, the European Commission and the Association of Manufacturers and Formulators of Enzyme Products (AMFEP),[5] it was agreed that joint dossiers will be split into individual data packages.

The current opinion addresses one data package originating from the joint dossier EFSA-Q-2015-00237. This data package, identified as EFSA-Q-2022-00429, concerns the food enzyme rennet containing chymosin and pepsin A from calves, young goats, lambs and buffaloes and submitted by Caglificio Clerici S.p.A.

2 | DATA AND METHODOLOGIES

2.1 | Data

The applicant has submitted a dossier in support of the application for authorisation of the food enzyme rennet containing chymosin and pepsin A from the abomasum of calves, young goats, lambs and buffaloes.

Additional information was requested from the applicant during the assessment process on 15 September 2023 and received on 8 November 2023 (see 'Documentation provided to EFSA').

2.2 | Methodologies

The assessment was conducted in line with the principles described in the EFSA 'Guidance on transparency in the scientific aspects of risk assessment' (EFSA, 2009b) and following the relevant existing guidance documents of EFSA Scientific Committee.

The 'Guidance on the submission of a dossier on food enzymes for safety evaluation' (EFSA, 2009a) has been followed for the evaluation of the application with the exception of the exposure assessment, which was carried out in accordance with the updated 'Scientific Guidance for the submission of dossiers on food enzymes' (EFSA CEP Panel, 2021).

3 | ASSESSMENT

The food enzyme under application contains two declared activities: chymosin and pepsin A.

IUBMB nomenclature	Chymosin
Synonyms	Rennin
IUBMB no	3.4.23.4
CAS no	9001-98-3
EINECS no	232-645-0

Chymosins are aspartic endopeptidases that catalyse the hydrolysis of the 104-Ser-Phe-/-Met-Ala-107 bonds of κ-casein, resulting in the destabilisation of casein micelles and causing milk to clot.

IUBMB nomenclature	Pepsin A
Synonyms	Pepsin; lactated pepsin; pepsin fortior; fundus-pepsin
IUBMB no	3.4.23.1
CAS no	9001-75-6
EINECS no	232-629-3

Pepsin A is also an aspartic endopeptidase which hydrolyses peptide bonds in proteins and peptide molecules with the formation of shorter peptides and free amino acids. It preferably cleaves peptide bonds between hydrophobic and aromatic amino acids.

The food enzyme is intended to be used in the production of cheese.

[4]Commission Implementing Regulation (EU) No 562/2012 of 27 June 2012 amending Commission Regulation (EU) No 234/2011 with regard to specific data required for risk assessment of food enzymes Text with EEA relevance. OJ L 168, 28.6.2012, p. 21–23.

[5]The full detail is available at the https://www.efsa.europa.eu/en/events/event/ad-hoc-meeting-industry-association-amfep-joint-dossiers-food-enzymes

3.1 | Source of the food enzyme

The food enzyme rennet is obtained from the abomasum of suckling calves (*Bos taurus*), goats (*Capra hircus*), lambs (*Ovis aries*) and buffaloes (*Bubalus bubalis*) from certified European and non-European suppliers,[6] surveyed and approved by the competent authorities. The food enzyme is exclusively obtained from healthy animals slaughtered under the supervision of official health authorities, following the requirements of the relevant EU hygiene regulations, the Food Hygiene Regulation (EC) No 852/2004[7] and Regulation (EC) No 853/2004.[8] Examples of certificates from non-European slaughterhouses were provided by the applicant, confirming that animal tissues used for the preparation of the food enzyme comply with meat inspection requirements and are handled in accordance with good hygienic practice.[9]

In the EU, according to Regulation (EC) 1069/2009,[10] the abomasum of calves, goats, lambs and buffaloes is considered fit for human consumption and is an edible offal as defined in Regulation (EC) No 853/2004.[11]

No issues of concern arising from the safety of the source material were identified by the Panel.

3.2 | Production of the food enzyme

The food enzyme is manufactured according to the Food Hygiene Regulation (EC) No 852/2004,[12] with food safety procedures based on Hazard Analysis and Critical Control Points, and in accordance with current Good Manufacturing Practice.[13]

The food enzyme is extracted from the abomasum of suckling calves, goats, lambs or buffaloes. After the animals are slaughtered, the abomasa are trimmed to remove unwanted tissues, emptied and then frozen. The abomasa are minced and macerated in a salt-water solution to extract the enzymes. The liquid fraction is sieved to remove any insoluble biomass and obtain a crude extract containing the food enzymes. Salt and acid are added to the clarified solution to reach an adequate pH to activate the two declared enzymatic activities. The extract is neutralised by increasing the pH and further clarified by flocculation. After a vacuum filtration that removes the remaining insoluble material and concentration by ultrafiltration, the extract is standardised.[14] Authorised preservatives may be added to the enzyme concentrate.[15]

The applicant provided information on the identity of the substances used in the extraction and in the subsequent downstream processing.[16]

The Panel considered that sufficient information has been provided on the manufacturing process and the quality assurance system implemented by the applicant to exclude issues of concern.

3.3 | Characteristics of the food enzyme

3.3.1 | Properties of the food enzyme

The chymosin from the abomasum of suckling calves, goats, lambs and buffaloes is a single polypeptide chain of 381 amino acids.[17] The molecular mass was calculated to be 36.5 kDa (Kumar et al., 2010).[18] The pepsin A from the abomasum of calves, young goats, lambs and buffaloes is a single polypeptide chain of 386 amino acids.[19] The molecular mass was calculated to be 35.0 kDa (Munoz et al., 2004).[20] No other enzymatic activities were reported.[21]

The determination of the chymosin and pepsin activities is based on the official method ISO 11815|IDF 157 (2007).[22] The time needed for visual flocculation of a standard milk substrate prepared with a calcium chloride solution of 0.5 g/litre (pH ≈ [redacted]) is determined. The clotting time of the rennet sample is compared to that of a bovine rennet reference standard

[6]Technical dossier/p. 43–44/Annexes 10–11.

[7]Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs. OJ L 139, 30.4.2004, pp. 54.

[8]Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for food of animal origin. OJ L226, 25.6.2004, p. 22.

[9]Technical dossier/Annexes 10–11.

[10]Regulation (EC) No 1069/2009 of the European Parliament and of the Council of 21 October 2009 laying down health rules as regards animal by-products and derived products not intended for human consumption and repealing Regulation (EC) No 1774/2002 (Animal by-products Regulation).

[11]Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for food of animal origin. OJ L226, 25.6.2004, p. 22.

[12]Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs. OJ L 139, 30.4.2004, pp. 54.

[13]Technical dossier/Annexes 12–13.

[14]Technical dossier/p. 46–53.

[15]Technical dossier/p. 48–49, 52.

[16]Technical dossier/p. 46/Annex 14.

[17]Technical dossier/p. 37.

[18]Technical dossier/p. 36; Brenda database.

[19]Technical dossier/p. 37.

[20]Technical dossier/p. 36; Brenda database.

[21]Technical dossier/p. 9, 34, 39.

[22]Technical dossier/p. 34, 39, 52-53/Annex 8.

with a known milk-clotting activity.[23] The total milk-clotting activity of both enzymes is expressed in IMCU (International Milk-Clotting Units).

The food enzyme has a pH optimum around 6.5 and a temperature optimum around 45°C. This activity decreased above 50°C, showing no residual activity above 65°C.[24]

3.3.2 | Chemical parameters

Data on the chemical parameters of the food enzyme were provided for eight batches used for commercialisation, three from calves, three from suckling goats, one from lambs and one from suckling buffaloes (Table 1). The applicant states that the rennets obtained from different species of animals are not blended.[25] The mean total organic solids (TOS) were 1.3%, 2.8%, 2.6% and 2.0%, respectively, and the mean enzyme clotting activities/mg TOS ratio were 17.2, 5.2, 6.1 and 9.2 IMCU/mg TOS, respectively.[26]

TABLE 1 Composition of the food enzyme rennet from the abomasum of different farm animals.

		Calves			Suckling goats			Lambs	Suckling buffaloes
Parameters	**Unit**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**1**
Milk clotting activity	IMCU/g[a]	184	99	184	169	155	112	160	184
Protein	%	1.1	1.4	1.5	3.2	2.3	1.9	2.6	1.2
Ash	%	18.4	17.3	17.8	16.5	17.1	17.4	16.0	17.3
Water	%	80.5	80.4	81.6	80.3	80.0	80.3	81.4	80.7
Total organic solids (TOS)[b]	%	1.1	2.3	0.6	3.2	2.9	2.3	2.6	2.0
Milk clotting activity/TOS ratio	IMCU/mg TOS	16.7	4.3	30.7	5.3	5.4	4.9	6.1	9.2

[a]IMCU: International Milk Clotting Unit (see Section 3.3.1).

[b]TOS calculated as 100% – % water – % ash.

3.3.3 | Purity

The lead content was measured in eight commercial batches: the levels were below 0.01 mg/kg in six batches, and 0.05 and 0.06 mg/kg in two batches.[27,28] The result complies with the specification for lead (5 mg/kg) as laid down in the general specifications for enzymes used in food processing (FAO/WHO, 2006).

The microbiological analyses of eight commercial batches were reported.[29] The results comply with the microbiological criteria for total coliforms, *Escherichia coli* and *Salmonella*, as laid down in the general specifications for enzymes used in food processing (FAO/WHO, 2006). Numbers of Enterobacteriaceae, *Campylobacter jejuni*, *Campylobacter coli*, *Escherichia* coli, *Listeria monocytogenes*, filamentous fungi and yeasts were also reported and raised no concern.

The Panel considered that the information provided on the purity of the food enzyme was sufficient.

3.4 | Toxicological data

According to the Commission Implementing Regulation (EU) No 562/2012,[30] an application for the safety evaluation of a food enzyme does not need to include toxicological data, if the food enzyme is obtained from edible parts of animals intended or reasonably expected to be ingested by humans.

According to the EFSA Guidance on the submission of a dossier on food enzymes for safety evaluation, the justification for not supplying toxicological data may include a documented history on the safety of the source of the food enzyme, the composition and the properties of the food enzyme, as well as its use in foods, demonstrating no adverse effects on human health when consumed in a comparable way (EFSA CEP Panel, 2021).

The Panel considered that these requirements are fulfilled, because:

[23]Technical dossier/p. 33/Annex 8.

[24]Technical dossier/p. 39–40/Annex 8.

[25]Technical dossier/p. 47.

[26]Technical dossier/p. 33/Annex 1–4, Annex 15–18.

[27]Technical dossier/p. 35/Annexes 1–4, Annexes 15-18/Annex 27.

[28]LoQ/LoD: Pb = 0.01 mg/kg.

[29]Technical dossier/p. 35/Annexes 1–4, Annexes 15-18/Annexes 19–26.

[30]Commission Implementing Regulation (EU) No 562/2012 of 27 June 2012 amending Commission Regulation (EU) No 234/2011 with regard to specific data required for risk assessment of food enzymes. OJ L 168, 28.6.2012, p. 21–23.

(i) rennet obtained from the abomasum of suckling calves, goats, lambs and buffaloes has been safely used in the production of cheese and related products for many centuries;
(ii) the abomasum from suckling calves, goats, lambs and buffaloes is consumed throughout the EU and elsewhere in the world as a meat product;
(iii) the manufacturing process of the food enzyme is not considered to introduce substances that could raise safety concerns;
(iv) the compositional and purity data provided on the food enzyme are considered sufficient.

The Panel considered that sufficient information was provided on the animal source, its history of safe use and consumption, and the manufacturing process. Therefore, the need for toxicological data was waived.

3.4.1 | Allergenicity

The potential allergenicity of the food enzyme containing chymosin and pepsin A derived from the abomasum of suckling calves, goats, lambs and buffaloes was assessed by comparing the amino acid sequence in full length with those of known allergens using different databases, and two matches were found.[31] The matching allergens was Sus s Pepsin and Bos d chymosin known as occupational respiratory allergens.

Cattle, sheep, goat and buffalo are not sources included in the list of substances or products causing allergies or intolerances (Regulation (EU) No 1169/2011[32]). Proteins from bovine abomasum are not known to be food allergens. Occupational respiratory allergies and skin sensitisation to dust of chymosin and pepsin A have been described in workers upon industrial exposure and in medical laboratory technicians (Cartier et al., 1984; Khan and Selamoglu, 2020; Jensen et al., 2006; van Kampen et al., 2013; Gómez Torrijos et al., 2018). However, several studies have shown that adults with occupational asthma can commonly ingest the corresponding respiratory allergens without acquiring clinical symptoms of food allergy (Armentia et al., 2009; Brisman, 2002; Cullinan et al., 1997; Poulsen, 2004). There are no reports in the literature on adverse reactions upon ingestion of these enzymes in individuals sensitised through the respiratory route.

The Panel considered that the risk of allergic reactions upon dietary exposure to this food enzyme cannot be excluded, but the likelihood is low.

3.5 | Dietary exposure

3.5.1 | Intended use of the food enzyme

The food enzyme is intended to be used in the production of cheese at the maximum recommended use level of 16 mg TOS/kg milk.[33]

Animal rennet is added to milk to separate milk into solid curd and liquid whey (coagulation). Both chymosin and pepsin contribute to the milk-clotting activity.[34] The majority of the food enzyme–TOS partitions into the whey and is mostly removed during the draining of the whey.[35] Only a small portion of the food enzyme–TOS remains in the curd (~ 10%). The remaining rennet contributes to the ripening of cheese due to its general proteolytic activity.[36]

Based on data provided on thermostability (see Section 3.3.1), it is expected that the food enzyme may remain active in cheese, depending on the cheese-making process.

3.5.2 | Dietary exposure estimation

The technology of extracting enzymes from animal abomasum and the technology of using animal rennet for making cheese have remained the same over thousands of years and remains the major source of human exposure to the food enzyme. Cheese has been consumed by humans in Europe and many other parts of the world for millennia. In addition, abomasum from ruminants is consumed in some European countries, which constitutes a minor fraction of the overall exposure to the food enzyme in the EU.

The Panel decided that a dietary exposure estimation was not required.

[31]Technical dossier/p. 66–67.

[32]Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004.

[33]Technical dossier/p. 12, 58.

[34]Technical dossier/p. 9, 11, 17.

[35]Technical dossier/p. 57, 73–74.

[36]Technical dossier/p. 9, 11, 17.

3.6 | Margin of exposure

Since no toxicological assessment and no dietary exposure estimation were considered necessary by the Panel, a margin of exposure was not calculated.

4 | CONCLUSION

Based on the data provided, the origin of the food enzyme and its history of safe use, the Panel concluded that the food enzyme rennet containing chymosin and pepsin A obtained from the abomasum of suckling calves, goats, lambs and buffaloes does not give rise to safety concerns under the intended conditions of use.

5 | DOCUMENTATION AS PROVIDED TO EFSA

Application for authorisation of Animal rennet from *Bos primigenius* (cattle), *Bubalus bubalis* (buffalo), *Capra aegagrus hircus* (goat) *and Ovis aries* (sheep) in accordance with Regulation (EC) No 1331/2008. June 2022. Submitted by Caglificio Clerici S.p.A.

Additional information. November 2023. Submitted by Caglificio Clerici S.p.A.

ABBREVIATIONS

CAS	Chemical Abstracts Service
EFSA CEP Panel	EFSA Panel on Food Contact Materials, Enzymes and Processing Aids
EINECS	European Inventory of Existing Commercial Chemical Substances
FAO	Food and Agricultural Organization of the United Nations
IDF	International Dairy Federation
IMCUS	International Milk-Clotting Units
ISO	International Organization for Standardization
IUBMB	International Union of Biochemistry and Molecular Biology
JECFA	Joint FAO/WHO Expert Committee on Food Additives
kDa	kiloDalton
LOD	limit of detection
LOQ	limit of quantification
TOS	total organic solids
WHO	World Health Organization

CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2022-00429

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NOTE

The full opinion will be published in accordance with Article 12 of Regulation (EC) No 1331/2008 once the decision on confidentiality will be received from the European Commission.

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REFERENCES

Armentia, A., Dıaz-Perales, A., Castrodeza, J., Duenas-Laita, A., Palacin, A., & Fernandez, S. (2009). Why can patients with baker's asthma tolerate wheat flour ingestion? Is wheat pollen allergy relevant? *Allergologia et Immunopathologia*, *37*(4), 203–204. https://doi.org/10.1016/j.aller.2009.05.001

Brisman, J. (2002). Baker's asthma. *Occupational and Environmental Medicine*, *59*(7), 498–502. quiz 502, 426.

Cartier, A., Malo, J.-L., Pineau, L., & Dolovich, J. (1984). Occupational asthma due to pepsin. *Journal of Allergy and Clinical Immunology*, *73*(5), 574–577. https://doi.org/10.1016/0091-6749(84)90513-X

Cullinan, P., Cook, A., Jones, M., Cannon, J., Fitzgerald, B., & Taylor, A. J. (1997). Clinical responses to ingested fungal alpha-amylase and hemicellulase in persons sensitized to *aspergillus fumigatus*? *Allergy*, *52*(3), 346–349. https://doi.org/10.1111/j.1398-9995.1997.tb01003.x

EFSA (European Food Safety Authority). (2009a). Guidance of EFSA prepared by the scientific panel of food contact material, enzymes, Flavourings and processing aids on the submission of a dossier on food enzymes. *EFSA Journal*, *7*(8), 1305. https://doi.org/10.2903/j.efsa.2009.1305

EFSA (European Food Safety Authority). (2009b). Guidance of the scientific committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: General principles. *EFSA Journal*, *7*(5), 1051. https://doi.org/10.2903/j.efsa.2009.1051

EFSA CEP Panel (EFSA Panel on Food Contact Materials, Enzymes and Processing Aids), Lambré, C., Barat Baviera, J. M., Bolognesi, C., Cocconcelli, P. S., Crebelli, R., Gott, D. M., Grob, K., Lampi, E., Mengelers, M., Mortensen, A., Rivière, G., Steffensen, I.-L., Tlustos, C., Van Loveren, H., Vernis, L., Zorn, H., Glandorf, B., Herman, L., … Chesson, A. (2021). Scientific guidance for the submission of dossiers on food enzymes. *EFSA Journal*, *19*(10), 6851. https://doi.org/10.2903/j.efsa.2021.6851

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). (2006). General specifications and considerations for enzyme preparations used in food processing in compendium of food additive specifications. 67th meeting. *FAO JECFA Monographs*, *3*, 63–67. https://www.fao.org/3/a-a0675e.pdf

Gómez Torrijos, E. G., Rodriguez, C. G., Pérez, B. V., Bartolomé, B., Barragan, M. P., & Rodriguez, R. G. (2018). Occupational allergic respiratory disease (rhinoconjunctivitis and asthma) in a cheese factory worker. Journal of allergy and clinical immunology. *In Practice*, *6*(4), 1416–1417. https://doi.org/10.1016/j.jaip.2017.12.009

ISO 11815|IDF 157. (2007). Milk – Determination of total milk-clotting activity of bovine rennets. https://fil-idf.org/publications/standards/milk-determination-of-total-milk-clotting-activity-of-bovine-rennets/

Jensen, A., Dahl, S., Sherson, D., & Sommer, B. (2006). Respiratory complaints and high sensitization rate at a rennet-producing plant. *American Journal of Industrial Medicine*, *49*(10), 858–861. https://doi.org/10.1002/ajim.20378

Khan, U., & Selamoglu, Z. (2020). Use of enzymes in dairy industry: A review of current Progress. *Archives of Razi Institute*, *75*(1), 131–136. https://doi.org/10.22092/ari.2019.126286.1341

Kumar, A., Grover, S., Sharma, J., & Batish, V. K. (2010). Chymosin and other milk coagulants: Sources and biotechnological interventions. *Critical Reviews in Biotechnology*, *30*(4), 243–258. https://doi.org/10.3109/07388551.2010.483459

Munoz, R., Garcia, J. L., Carrascosa, A. V., & Gonzales, R. (2004). Cloning of the authentic bovine gene encoding pepsinogen a and its expression in micro-bial cells. *Applied and Environmental Microbiology*, *70*(5), 2588–2595. https://doi.org/10.1128/aem.70.5.2588-2595.2004

Poulsen, L. K. (2004). Allergy assessment of foods or ingredients derived from biotechnology, gene-modified organisms, or novel foods. *Molecular Nutrition and Food Research*, *48*(6), 413–423. https://doi.org/10.1002/mnfr.200400029

van Kampen, V., Lessmann, H., Brüning, T., & Merget, R. (2013). Occupational allergies against pepsin, chymosin and microbial rennet. *Pneumologie*, *67*(5), 260–264. https://doi.org/10.1055/s-0032-1326407

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