Australian Government
Department of Health
Therapeutic Goods Administration

Compositional guideline for Protease

Name of the ingredient

Protease (ABN)

Definition of the ingredient

CAS Number: 9001-92-7

Proteases (both endo- and exo- types with no systemic name) are enzymes that are commercially derived from the fungus, *Aspergillus oryzae or Aspergillus niger*, via a fermentation process. During the recovery phase of production, manufacturers destroy *A. oryzae* or *A. niger*, before removing the non-proteinaceous material away from the protease preparation. Proteases are recovered from the fermentation broth in an aqueous solution and then processed to a dried state.

Table 1. Ingredient specific requirements

Test	Method reference	Acceptance criteria
Description		
Appearance	Visual	Powder
Characteristics		
Loss on drying (determined on 0.5 g by drying at 60°C at a pressure not exceeding 670Pa for 4 h)	BP (Appendix IX D); Ph Eur method 2.2.32	No more than 5%
Identification		
Protease activity	FCC	Complies
Assay		
Protease activity	FCC	No less than 85.0% but no more than 115.0% of the declared activity expressed as HUT*

Test	Method reference	Acceptance criteria
Notes		
*HUT = haemoglobin units on the tyrosine basis		

Table 2. Incidental constituents

Test	Method reference	Acceptance criteria
Incidental metals and non-metals		
While ingredient manufacturers are encouraged to include limits for Incidental metals and non-metals, it is the product into which those substances are formulated that contains the ingredient, alone or in combination with other ingredients, must comply with the acceptance criteria set in the United States Pharmacopeia - National Formulary general chapter '<2232> Elemental Contaminants in Dietary Supplements'. When testing is performed at the raw material stage, calculation of the total daily exposure in the finished product should be performed. This calculation is based on the quantity of each ingredient present in the product, the maximum potential contamination given the proposed limits for each raw material and the daily dose of the product.		
Other organic or inorganic impurities or toxins		
Mycotoxins and aflatoxins	FCC, AOAC	Not detected
Antibiotic activity	JECFA	Not detected
Microbiology		
While substance manufacturers are encouraged to include limits for objectionable microorganisms, it is the product into which those substances are formulated that is subject to a legally binding set of criteria. The Therapeutic Goods Order No. 77 *'Microbiological Standards for Medicines'* mandates that any finished product that contains the ingredient, alone or in combination with other ingredients, must comply with the microbial acceptance criteria set by Clause 9 of the Order.		

Key to abbreviations: - insert or delete as required

AOAC = Association of Analytical Communities Official Methods of Analysis 16th Ed. AOAC

BP = British Pharmacopoeia

FCC = Food Chemicals Codex

JECFA = Joint FAO/ WHO Expert Committee on Food Additives in FAO Food and Nutrition Paper No.52 (Addendum 9)

Ph Eur = European Pharmacopoeia