Hydrolysed Proteins

DOCUMENT M-CA, Section 5

TOXICOLOGICAL AND METABOLISM STUDIES ON THE ACTIVE SUBSTANCE

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

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CA 5 TOXICOLOGICAL AND METABOLISM STUDIES ON THE ACTIVE SUBSTANCE

Introduction

According to EFSA Journal 2012; 10(2):2545, it was concluded that "*hydrolysed proteins per se are likely to be of low toxicological concern provided hydrolysed proteins of animal origin are pathogen-free. On this basis no risks to human health could be expected from its use as a plant protection product and data waivers for specific toxicological studies were initially supported. However, due to the fact that a specification to include the main components in the active substances is still outstanding, a final conclusion cannot be drawn whether the technical specification is of toxicological concern and whether data waivers can be accepted*." A data gap was identified.

Considering the nature, origin, manufacturing process, composition and technical specifications of the Hydrolysed proteins as provided in Document J, there is no component of toxicological concern, thus confirming that hydrolysed proteins are of low toxicity.

Furthermore, Hydrolysed proteins are naturally occurring compounds of degradation from the hydrolysis of living organisms' tissues that can have vegetable or animal origin. The degradation of the hydrolysed proteins results in more simple metabolites called amino acids. Proteins and amino acids are abundant organic molecules in living cells. They can be found in every single cell, since they are fundamental in all aspects of the cell structure and function, and intervene in the most essential biochemical processes.
The proteins are one of the three basic principal nourishment of living beings. The proteins that are found in food and eaten by human beings and mammals are normally degraded metabolically by means of enzymatic processes and results in amino acids, that are then used by the living cells for the biosynthesis of new specific proteins.
Therefore, the hydrolysed proteins and resulting metabolites are not expected to cause any danger to human beings and mammals in general because as explained, these compounds take place in every living cells and are therefore essential for life.

Moreover, it should be noted that the review of the scientific literature within the last 10 years did not give any results indicating a hazardous effect or a potential risk for humans and mammals in general. Please refer to Document M-CA 9.

Furthermore, it should be noted that according to the notifications provided to ECHA in REACH registrations and CLP notifications, no hazards have been classified for the active substance Hydrolysed proteins, referred as "*Protein hydrolyzates, animal*" by ECHA. Please refer to the summary from ECHA provided in Document M-CA 10.

For all these reasons, the use of Hydrolysed proteins is considered to pose a low risk to operators, workers, bystanders and residents and no testing toxicity data are required.

CA 5.1 Studies on Absorption, Distribution, Metabolism and Excretion in Mammals

CA 5.1.1 Absorption, distribution, metabolism and excretion by oral exposure

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.1.2 Absorption, distribution, metabolism and excretion by other routes

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.2 Acute Toxicity

No EU endpoints available. According to EFSA Journal 2012; 10(2):2545, it was concluded that available data was of limited validity.

However, no new data is submitted, nor required. Please refer to the argumentation presented under Point B 5.

CA 5.2.1 Oral

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be classified for acute oral toxicity.

CA 5.2.2 Dermal

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be classified for acute dermal toxicity.

CA 5.2.3 Inhalation

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be classified for acute inhalation toxicity.

CA 5.2.4 Skin irritation

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern.

Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be skin corrosive.

CA 5.2.5 Eye irritation

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be irritant for eyes.

CA 5.2.6 Skin sensitisation

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to skin sensitizer.

CA 5.2.7 Phototoxicity

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.3 Short-Term Toxicity

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.3.1 Oral 28-day study

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.3.2 Oral 90-day study

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.3.3 Other routes

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.4 Genotoxicity Testing

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern and since their components have an essential role in living cells, it is deemed acceptable to consider that the active substance Hydrolysed proteins have no genotoxic potential.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be mutagenic.

CA 5.4.1 *In vitro* studies

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.4.2 *In vivo* studies in somatic cells

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.4.3 *In vivo* studies in germ cells

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.5 Long-Term Toxicity and Carcinogenicity

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern and since their components have an essential role in living cells, it is deemed acceptable to consider that the active substance Hydrolysed proteins have no carcinogenic potential.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be carcinogenic.

CA 5.6 Reproductive Toxicity

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern and since their components have an essential role in living cells, it is deemed acceptable to consider that the active substance Hydrolysed proteins have no reproductive toxicity.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be not toxic for reproduction.

CA 5.6.1 Generational studies

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.6.2 Developmental toxicity studies

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.7 Neurotoxicity Studies

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to its nature, origin and composition, Hydrolysed proteins are *per se* of low toxicological concern and since their components have an essential role in living cells, it is deemed acceptable to consider that the active substance Hydrolysed proteins are not neurotoxic.
Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be has neurotoxic effects.

CA 5.7.1 Neurotoxicity studies in rodents

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.7.2 Delayed polyneuropathy studies

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.8 Other Toxicological Studies

CA 5.8.1 Toxicity studies of metabolites

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.8.2 Supplementary studies on the active substance

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.8.3 Endocrine disrupting properties

No data submitted, not required. Please refer to the argumentation presented under Point B 5.
Due to the nature, origin and composition of the Hydrolysed proteins, whose components have an essential role in living cells, it is deemed acceptable to consider that the active substance Hydrolysed proteins have no endocrine disrupting properties.

Therefore, Hydrolysed Proteins meet the criteria for the approval of low-risk active substance because not considered to be an endocrine disruptor.

CA 5.9 Medical Data

No EU data/endpoints available.

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.9.1 Medical surveillance on manufacturing plant personnel and monitoring studies

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.9.2 Data collected on humans

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.9.3 Direct observations

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.9.4 Epidemiological studies

No data submitted, not required. Please refer to the argumentation presented under Point B 5.

CA 5.9.5 Diagnosis of poisoning (determination of active substance, metabolites), specific signs of poisoning, clinical tests

Specific signs of poisoning or clinical tests are not known nor not expected.

CA 5.9.6 Proposed treatment: first aid measures, antidotes, medical treatment

Due to the nature and low toxicity of Hydrolysed proteins, there is no special antidotes or medical treatment.

First aid measures:

- Eye contact: Rinse thoroughly with water.
- Inhalation: Go to fresh air. If symptoms appear, seek medical attention.
- Ingestion: Rinse the mouth with a lot of water. Consult a doctor if you feel unwell.
- Skin contact: Wash the affected area with water and soap, rinse thoroughly.
- Most important symptoms and effects, both acute and delayed: There is no knowledge of important symptoms and effects
- Indication of any immediate medical attention and special treatment needed: Not known.

CA 5.9.7 Expected effects of poisoning

Due to the nature and low toxicity of Hydrolysed proteins, there is no expected effects of poisoning.