View Notification

Draft ID	Filing Date	Category of Compound
ENZO001629	08/06/2018	

Section 1: Contact Information

Contacts List

Type	Name	Address
Submitter	Enzolytics, Inc.	120 W Pomona Ave, Monrovia, CA 91016-4557 United States
Owner	Enzolytics, Inc.	120 W Pomona Ave, Monrovia, CA 91016-4557 United States
Primary	Harry Zhabilov	120 W Pomona Ave, Monrovia, CA 91016-4557 United States

Submitter

Type of Submitter
Manufacturer of NDI
Distributor of NDI

Company Name *(if applicable)*
Enzolytics, Inc.

Mailing Address Line 1
120 W Pomona Ave

Mailing Address Line 2

Country
United States

ZIP or Postal Code
91016-4557

City
Monrovia

State or Province
CA

Owner

Type of Submitter
Manufacturer of NDI
Distributor of NDI

Company Name *(if applicable)*
Enzolytics, Inc.

Corrected Company Name

Mailing Address Line 1
120 W Pomona Ave

Mailing Address Line 2

Country
United States

ZIP or Postal Code
91016-4557

City
Monrovia

State or Province
CA

Primary

Type of Contact
Other - CEO, Inventor

First Name of Contact Person
Harry

Last Name of Contact Person
Zhabilov

Company Name
Enzolytics, Inc.

Position
CEO

Phone Number
001 310 4353967

Fax Number

Email Address
zhabilov@att.net

Mailing Address
120 W Pomona Ave

Country
United States

ZIP or Postal Code
91016-4557

City
Monrovia

State or Province
CA

Section 2: General Administrative Information

1. Name of the New Dietary Ingredient
Enzolytics Pepsin From Porcine Supplement Spray

2. Have you designated information in your notification that you view as a trade secret or as confidential commercial information?
No

3. Are you providing a redacted copy of some or all of the notification?
No

4. Are all citations to published information accompanied by reprints or full photostatic copies of the publications?
Yes

5. Are the notification and all publications submitted in English or accompanied by a complete and accurate English translation?
Yes

Section 3: Description of NDI and Dietary Supplement Containing the NDI

1. New Dietary Ingredient Type
Dietary substance for use by man to supplement the diet by increasing the total dietary intake

2. Name of the new dietary ingredient and related information
Maximum level of new dietary ingredient in each serving of dietary supplement (include units)

1 ml Serving Size 7 Sprays

NDI Name **Enzolytics Pepsin From Porcine Supplement Spray**	Latin Binomial Name (LBN)
	Correcetd Latin Binomial Name (LBN)
Corrected NDI Name	Author of LBN
Synonyms and Trade Name	Corrected Author of LBN
Corrected Synonyms and Trade Name	
Plant Part and Strain	

3. Dietary supplement serving form
Liquid

4. Description of dietary supplement (Include the level of NDI and all other ingredients in one unit of the dietary supplement. If the notification concerns an NDI that is a combination of two or more other NDIs, you should provide the following information for each component NDI: Synonyms, Trade Name, Plant Part, Strain, Latin Binomial Name, Author of Latin Binomial Name, and NDI type. Where relevant, also include the following additional information: CAS registry number, Unusual form (e.g., malted barley or immature apples), Type of manufacture (e.g., greater than 99% purity, 50:1 dry leaf extract, or fermentation product)).
Irreversible Pepsin Fraction (IPF) from Porcine 4.0 mg/ml, Sodium Chloride -USP/NF 4.5 mg/ml, Sodium Acetate - Anhydus USP/NF 3.4 mg/ml, Sodium Citrate .5mg/ml, Sulfate .5mg/ml

5. Conditions of Use of the Dietary Supplement

5a. Serving instructions (e.g., "take with food", "take before bed", "dissolve in a glass of water", etc).
Shake well before use as dietary supplement. Spray 7 times in oral cavity and digest two days a week before breakfast for eight weeks. Rest one week, Repeat process, up to three times.

5b. Dietary supplement serving size (weight or volumetric measure), serving frequency (# of servings/day, interval between servings), duration of use and maximum total daily intake level
1 ml from 7 sprays taken before Breakfast twice a week on consecutive days for eight weeks. Rest on the ninth week. Repeat the process up to three cycles.

5c. Target populations / excluded populations / other restrictions
All individuals can benefit from this treatment

Section 4: Safety Information Attachment

Attachment

Name of Attachment
Enzolytics FDA APP COMPLETE (2).pdf (fileDownload.htm?module=NDI&fileIdEnc=L3UwNC9mdXJsc1VwbG9hZC8vYmNjMzFhMGEtYjAzYS00M2Q3LTg1ZDEtYTgyYmFmNjNlMmQ4L0Vuem9seXRpY3MgRkRBIEFQUCAgQ09NUExFVE UgKDIpLnBkZg==&fileId=31b5-4bb9-8e5d-1eabefdcb232)

Section 5: Additional Attachments

Attachment(s)

There are no attachments uploaded in this section.

Section 6: Certification

Name of Submitter
Harry H. Zhabilov

Title of Submitter
CEO

I certify that the information in the notification is true and accurate and that I am authorized to submit the notification on behalf of the notification owner.

☑ **I Agree.**

NEW DIETARY INGREDIENT (NDI) SAFETY INFORMATION

ENZOLYTICS, INC.
August 4th, 2018

Instructions

- In this template, which supplements the data entry screens in the NDI notification electronic submission portal, you will describe the scientific information on which you base your conclusion that the dietary supplement containing the NDI will reasonably be expected to be safe. Safety information includes, among other things, (1) information showing that the NDI is identical or related to substances documented as having a history of use as food; (2) information showing that the NDI is identical or related to test articles used in safety studies; (3) information showing that a substance or product has a history of use as food; and (4) safety data, including the results of genetic toxicology studies, pharmacokinetic studies, animal toxicology studies and human clinical studies. This template asks for details about the identity of the NDI, verification of that identity, information about history of use as food, and any other evidence relevant to the safety of the NDI under its proposed conditions of use in the dietary supplement. After filling in the template, you will upload the completed template as an attachment to your online NDI notification and attach files containing the scientific publications cited in your notification.

- For a notification that concerns the use of an NDI in a dietary supplement that contains no other ingredients, the safety of the NDI and the dietary supplement would be synonymous.
In other situations, however, that may not be the case. For example, when an NDI is used in a dietary supplement with one or more other NDIs, the safety of the dietary supplement may not be the sum of the safety of the individual NDIs. In such circumstances, you should document your basis for concluding that the dietary supplement will reasonably be expected to be safe and explain why that conclusion is reasonable. For example, if two botanical extracts have separate histories of use in traditional medicine, but no history of being used together, the safety of the combination may not be clear from the safety information pertaining to the individual NDIs. On the other hand, if an extract of a medicinal herb is combined with an extract of a material that has a long history of safe use as food, then it may be reasonable to conclude that the combination is safe based on information about the safety of the individual NDIs. If you wish to submit a notification for the use of an NDI in a dietary supplement with other NDIs, the FDA recommends that you confer with a member of the New Dietary Ingredient Review Team in FDA's Division of Dietary Supplement Programs about how to proceed. If you have any questions concerning this matter please contact the New Dietary Ingredients Review Team, which can be reached on (240) 402-1756 or by email at fred.hines@fda.hhs.gov.

- If a section or subsection is not applicable to your notification, mark "N/A" in your response.

- Sections marked as "Required" in the template's section headings must have complete responses in all subsections for which you have data. If you leave a "Required" section blank or respond "N/A," FDA will consider your notification incomplete for failure to comply with 21 CFR 190.6(b). An incomplete notification does not satisfy the requirement

to submit an NDI notification. You may not introduce your NDI or a dietary supplement containing the NDI into interstate commerce, or deliver the NDI or dietary supplement for introduction into interstate commerce, until at least 75 days after you have submitted a complete notification to FDA.

- Please include full citations for all published and unpublished sources cited or relied on in your notification in the Reference List (Section 5). You will be prompted to attach e-copies of these sources when you return to the electronic submission portal after filling in this template.

- The template includes some sections identified as "Recommended." These sections solicit information that FDA considers helpful in evaluating NDI notifications. You are encouraged but not required to respond to template sections that are identified as "Recommended." However, if you leave a "Recommended" section blank or respond "N/A" and FDA determines that the information is needed to establish safety, your notification may be considered inadequate to conclude that the NDI will reasonably be expected to be safe under its proposed conditions of use in the dietary supplement.

Table of Contents

1. New Dietary Ingredient Identity Information (Recommended)

Enzolytics Pepsin from Porcine Supplemental Spray

1.1 Description of the identity of the NDI

A suspension of Inactivated Pepsin Fragment that comes from the purified extract of Pepsin from Porcine gastric mucosa powder, this compound is basically a chain of amino acids in a liquid form to be ingested orally via spray applicator. The compound contains Pepsin from Porcine, Sodium Chloride, as dietary ingredients and other ingredients such as Sodium Citrate, and Sulfates as preservatives and Sodium Acetate that serves as a buffering agent.

1.2 Description of the evidence verifying the identity of the NDI

We verify the identity of this NDI in basically four documents of which we have enclosed copies:

The first one relates to the actual extraction from porcine, these procedures are stablished in the document called: *Pepsin extraction process from swine* published in August 2012 at the 20th International Congress of Chemical and Process Engineering CHISA by authors E. Jurado a*, J. M. Vicaria, M. Lechuga, I. Moya-Ramírez of the Department of Chemical Engineering, Faculty of Sciences, University of Granada, Spain.

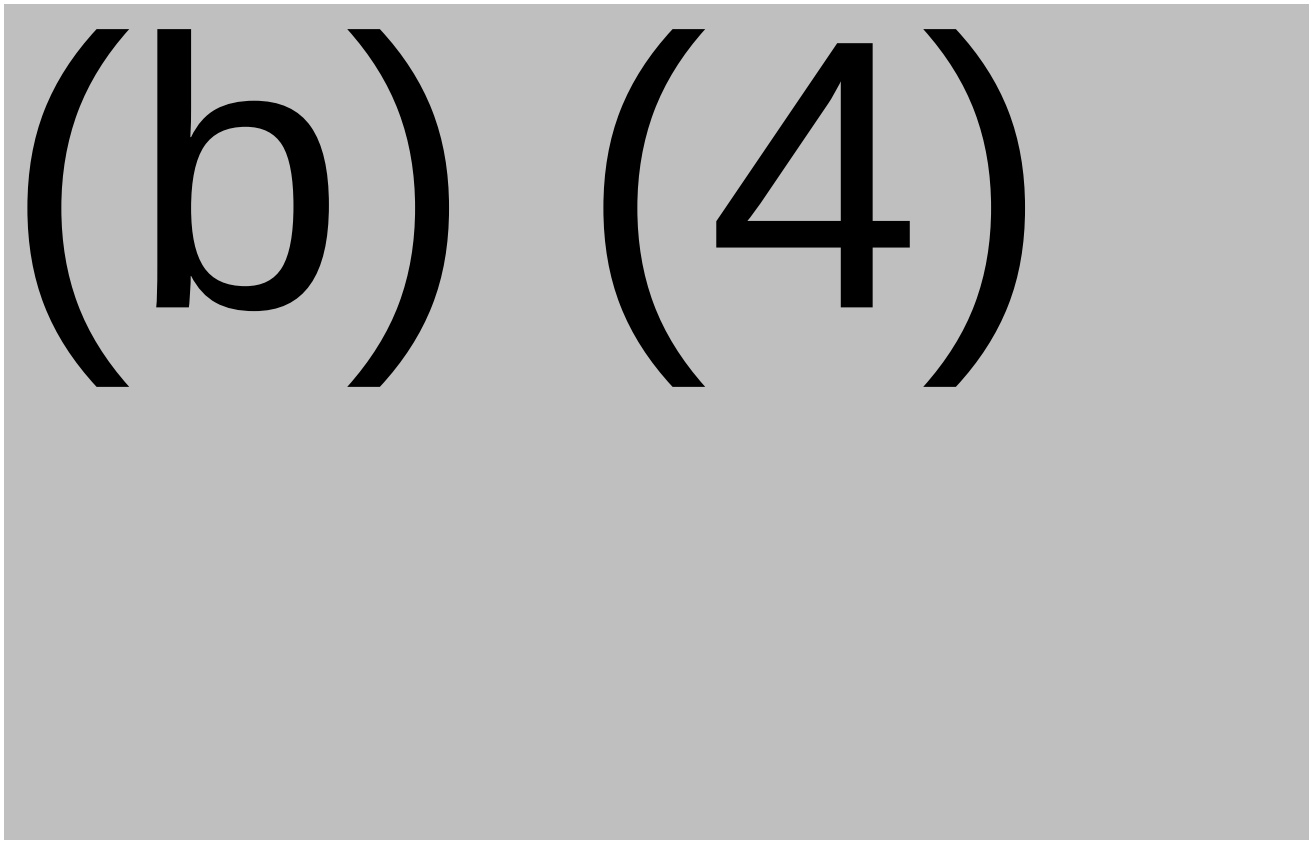
The second one illustrates the profound scientific research and development of pepsin as a commonly use for human on a diversity o ways with consistency and safety, this document is: *Inactivated pepsin inhibits neutrophil activation by Fcgamma-receptor-dependent and independent stimuli,* presented by Iwan Kustiawan, Ninotska Derksen, Theo Rispens from the Sanquin Research, Department of Immunopathology, and the Landsteiner Laboratory, Academic Medical Centre, University of Amsterdam, The Netherlands

The third one comes from Sigma Aldrich for the Pepsin from Porcine Gastric mucosa powder product P-7000 specification sheet as provided by this company.

The fourth document referring to the extract or amino acid chain Inactivated Pepsin Fragment that is listed under US Patent Number: US 7479538 Document Kind: B2 Patent Title: Irreversibly-inactivated pepsinogen fragment Named Inventors: ZHABILOV HARRY H Applicants (Assignees): ZHABILOV TRUST Agents: Cislo & Thomas, LLP Filing Date: 7/11/2005 Issue/Pub Date: 1/20/2009 Patent Termination: Expires: 7/11/2025.

1.3 NDI manufacture

Enzolytics Pepsin from Porcine Supplemental Spray is commercialized and distributed by Enzolytics Inc. and manufactured by:



We have enclosed for this point two documents a presentation of the manufactures and a copy of its drug manufacturing license.

1.3.1 Raw materials

(b) (4)

1.3.2 Formulation ingredients

(b) (4)

(b) (4)

1.3.4 NDI specifications

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

2. Dietary Supplement Manufacture (Recommended)

NOT APLICABLE

2.1. Raw materials.

NOT APLICABLE

2.2. Formulation ingredients other than the NDI

NOT APLICABLE

2.3. Manufacturing process

NOT APLICABLE

2.4. Product specifications

NOT APLICABLE

2.5. Methods of analysis

NOT APLICABLE

2.6. Analysis of potentially toxic processes

NOT APLICABLE

2.7. Disintegration and dissolution profile

NOT APLICABLE

2.8. Shelf-life and conditions of storage

NOT APLICABLE

3. History Of Use Or Other Evidence Of Safety (Required)

3.1 History of use

Studies on gastric digestion during 1820–1840 led to the discovery of pepsin as the agent which, in the presence of stomach acid, causes the dissolution of nutrients such as meat or coagulated egg white. Soon afterward it was shown that these protein nutrients were cleaved by pepsin to diffusible

products named peptones. Efforts to isolate and purify pepsin were spurred by its widespread adoption for the treatment of digestive disorders, and highly active preparations were available by the end of the nineteenth century. There was uncertainty, however, as to the chemical nature of pepsin, for some preparations exhibited the properties of proteins while other preparations failed to do so. The question was not settled until after 1930, when Northrop crystallized swine pepsin and provided convincing evidence for its identity as a protein. The availability of this purified pepsin during the 1930s also led to the discovery of the first synthetic peptide substrates for pepsin, thus providing needed evidence for the peptide structure of native proteins, a matter of debate at that time. After 1945, with the introduction of new separation methods, notably chromatography and electrophoresis, and the availability of specific proteinases, the amino acid sequences of many proteins, including pepsin and its precursor pepsinogen, were determined. Moreover, treatment of pepsin with chemical reagents indicated the participation in the catalytic mechanism of two aspartyl units widely separated in the linear sequence. Studies on the kinetics of pepsin action on long chain synthetic peptides suggested that the catalytic site was an extended structure. Similar properties were found for other “aspartyl proteinases,” such as chymosin (used in cheese making), some intracellular proteinases (cathepsins), and plant proteinases. After 1975, the three-dimensional structures of pepsin and many of its relatives were determined by means of x-ray diffraction techniques, greatly extending our insight into the mechanism of the catalytic action of these enzymes.

Abstract from journal article “A History Of Pepsin And Related Enzymes” Joseph S. Fruton *The Quarterly Review of Biology* Vol. 77, No. 2 (June 2002), pp. 127-147 Published by: The University of Chicago Press.

Pepsin from Porcine has been commonly used in nutritional supplements in many commercial brands and it is determined as safe for human consumption. Pepsin from Porcine 1:10,000 is classified under U.S. regulations: FDA - Food Additives Generally Recognized as Safe (GRAS): 21 CFR 184.159 FDA - 21 CFR - Total Food Additives 137.305 184.1595

3.1.1 Description of the relationship between the historically consumed material and the NDI or dietary supplement containing the NDI

(b) (4) , the relationship is quite direct because it is the same substance fundamentally.

3.1.2 Describe identity information verifying the relationship between the historically consumed material and the NDI or dietary supplement containing the NDI

The active ingredient is Irreversible Pepsin Fraction, which is an amino acid chain, the remaining components are residuals from the (b) (4) and the final product is (b) (4) .

We can verify the relation of Pepsin from Porcine to the NDI irreversible pepsin fraction, since both are integrated by chains of amino acids and being the same substance, for that we have enclosed the safety data sheet and product specification for Sigma Aldrich which sells Pepsin Porcine Powder.

3.1.3 Historical conditions of use and cumulative exposure estimate for the historically consumed material

Pepsin is a compound whose zymogen (pepsinogen) is released by the chief cells in the stomach and that degrades food proteins into peptides. It was the first enzyme to be discovered, and, in 1929, it became one of the first enzymes to be crystallized, by John H. Northrop. Pepsin is a digestive protease, a member of the aspartate protease family.

Pepsin is one of three principal protein-degrading, or proteolytic, enzymes in the digestive system, the other two being chymotrypsin and trypsin. The three enzymes were among the first to be isolated in crystalline form. During the process of digestion, these enzymes, each of which is specialized in severing links between particular types of amino acids, collaborate to break down dietary proteins into their components, i.e., peptides and amino acids, which can be readily absorbed by the intestinal lining. Pepsin is most efficient in cleaving peptide bonds between hydrophobic and preferably aromatic amino acids such as phenylalanine, tryptophan, and tyrosine.Joseph S. Fruton Yale University New Haven, Connecticut USA.

3.1.4 Adverse events associated with historically consumed material

- May cause a mild allergic skin reaction.
- May cause mild eye irritation if directly applied to them.
- May cause mild allergy or asthma symptoms

3.1.5 Alternative rationale for reasonable expectation of safety based on history of use

The adverse events stated in the last point are of very exceptional occurrence, the amounts applied and contained in our presentation are not sufficient to be constantly adverse but more of and exceptional event, reasonably no seriously adverse effects have been recorder, the cautions stated are intended for precaution of these exceptions, even so the consequences of their adverse effect are not transcendent or serious enough to cause any physical damage what so ever to tissue, organs or biological systems, as an example cleaning compounds for hair such as shampoo or soap may cause more irritability to skin and eyes than our compound because their components are chemically more complex and less natural.

3.2 Other evidence of safety

Code of Federal Regulations
Title 21, Volume 3
Revised as of April 1, 2017
CITE: 21 CFR184.1595

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER B--FOOD FOR HUMAN CONSUMPTION (CONTINUED)
PART 184 -- DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

Subpart B--Listing of Specific Substances Affirmed as GRAS
Sec. 184.1595 Pepsin.

(a) Pepsin (CAS Reg. No. 9001-75-6) is an enzyme preparation obtained from the glandular layer of hog stomach. It is a white to light tan powder, amber paste, or clear amber to brown liquid. Its characterizing enzyme activity is that of a peptide hydrolase (EC 3.4.23.1).

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of Food Additive Safety (HFS-200), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240-402-1200, and at the National Archives and Records Administration (NARA).

(c) In accordance with §184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as GRAS as a direct food ingredient is based upon the following current good manufacturing practice conditions of use:

(1) The ingredient is used as an enzyme as defined in §170.3(o)(9) of this chapter to hydrolyze proteins or polypeptides.

(2) The ingredient is used in food at levels not to exceed current good manufacturing practice.

[60 FR 32911, June 26, 1995, as amended at 78 FR 14667, Mar. 7, 2013]

3.2.1 Safety study type

Pepsin from porcine is an ingredient approved by the FDA as a GRAS (generally recognized as safe) substance under CFR Sec. 184.1595.
A substance may be GRAS only if its general recognition of safety is based on the views of experts qualified to evaluate the safety of the substance. GRAS status may be based either on a history of safe use in food prior to 1958 or on scientific procedures, which require the same quantity and quality of evidence as would be required to obtain a food additive regulation. Because GRAS status may be either affirmed by FDA or determined independently by qualified experts, FDA's regulations do not include all GRAS ingredients and the specific uses described in the GRAS regulations may not be comprehensive for the listed ingredients.

3.2.2 Safety study title, if any

NOT APLICABLE

3.2.3 Citation for the safety study (either public or non-public), if any

Pepsin (CAS Reg. No. 9001-75-6) CITE: 21 CFR184.1595

3.2.4 Identity information verifying the relationship between the test article and the NDI or the dietary supplement

Food Chemicals Codex, 3d ed. (1981), p. 110, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51.

3.2.5 Route of administration, serving size, frequency of use, interval between servings, and duration of use of the test article

NOT APLICABLE

3.2.6 Study design and safety metrics

NOT APLICABLE

3.2.7 Discussion of toxicity and conclusion

Since the discovery of pepsin from porcine and it has been deemed as a safe ingredient for human consumption as affirmed in CFR 184.1595 cite 21, this new ingredient is just a purified version that creates a particular chain of amino acids that are included with in the ones integrating pepsin form porcine and are know to be beneficial and safe for human consumption and can possibly be taken as a supplement in daily ingestion as it may support of the immune system.

3.2.8 Alternative rationale for reasonable expectation of safety based on other evidence of safety

Besides the safety regulations stated we conclude that the amounts of this substance and the liquid format it is presented can gives a reasonable expectation of safety due to the amounts a person can ingest at once even if deliberately overstating the recommended daily dosage and because it contains ingredients that have been extensively and for some time considered to be safe.

4. Basis For Concluding That the New Dietary Ingredient Will Reasonably Be Expected To Be Safe For Use in the Dietary Supplement (Required)

The scientific data and information about the use of this substance is widely known and there is a consensus among qualified experts that those data and information establish that the substance is safe under the conditions of its intended use. Pepsin from porcine is affirmed to have GRAS determinations which are made in this manner and said to be made through scientific procedures.

4.1 Determination of the No-Observed-Adverse-Effect-Level (NOAEL) or Lowest-Observed Adverse Effect Level (LOAEL)

We have no information on NOAEL or LOAEL.

4.2 Determination of safety factor

General recognition of safety through experience based on common use and a substantial history of consumption for food use by a significant number of consumers.

4.3 Determination of the Acceptable Daily Intake (ADI)

No acceptable daily intake has been determined.

4.4 Determination of Estimated Daily Intake (EDI) and the EDI/ADI Ratio

We determined our estimated daily intake based on common use and user convenience, 7 sprays to mouth cavity amounting to 1 ml, two consecutive days a week, totals 2 ml a week for 8 consecutive weeks summarizing 16 ml in 8 weeks, suspend for one week and repeat two 8 week series including in between suspension week for a total 48 ml. in 3 8 week series with one week suspended use between them, we observe that the ingest of pepsin from porcine should be in a moderate and balanced fashion, as with any nutritional or dietary intake in human consumption. We have no EDI/ADI ratio since no ADI has been determined.

4.5 Determination of margin of safety

Pepsin from porcine safety margins are generally accepted from a consensus of expert opinion regarding the safety of the use of the substance.

4.6 Safety narrative and conclusion

We consider the FDA definition of ‘safe' as 'a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use'

4.7 Alternative basis for reasonable expectation of safety

There are no alternative basis for expectation of safety but the ones stablished by FDA regulations particular to pepsin from porcine.

23 pages redacted under b4 internal research/analysis/studies

(b) (4)