EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Safety of the Food Chain
Chemicals, contaminants, pesticides

COMMISSION STAFF WORKING DOCUMENT[1]

Basic Substance
Chitosan hydrochloride
SANCO/12388/2013– rev. 2
20 March 2014

Final

Review report for the basic substance *Chitosan Hydrochloride*
Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 20 March 2014
in view of the approval of *Chitosan Hydrochloride* as basic substance in accordance with Regulation (EC) No 1107/2009

1. Procedure followed for the evaluation process

This review report has been established as a result of the evaluation of *Chitosan Hydrochloride* made in the context of the assessment of the substance provided for in Article 23 of Regulation (EC) No 1107/2009[2] concerning the placing of plant protection products on the market, with a view to the possible approval of this substance as basic substance.

In accordance with the provisions of Article 23(3) of Regulation (EC) No 1107/2009, the Commission received on 19 December 2011 an application from Chipro, hereafter referred to as the applicant, for the approval of the substance *Chitosan Hydrochloride* as basic substance.

The application and attached information were distributed to the Member States and European Food Safety Authority (EFSA) for comments. The applicant was also allowed to address collated comments and provide further information to complete the application, which was finalised in the new version of August 2012.

In accordance with the provisions of Article 23(4) of Regulation (EC) No 1107/2009 the Commission required scientific assistance on the evaluation of the application to EFSA, who delivered its views on the specific points raised in the commenting phase.

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1 Does not necessarily represent the views of the Commission.

2 OJ L 309, 24.11.2009, p. 1-50.

EFSA submitted to the Commission the results of its work in the form of a technical report for *Chitosan Hydrochloride* on 24 May 2013[3].

The Commission examined the application, the comments by Member States and EFSA and the EFSA Technical report on the substance together with the additional information and comments provided on it by the applicant, before finalising the current draft review report, which was referred to the Standing Committee on the Food Chain and Animal Health for examination. The draft review report was finalised in the meeting of the Standing Committee of 20 March 2014.

The present review report contains the conclusions of the final examination by the Standing Committee. Given the importance of the EFSA technical report, and the comments and clarifications submitted (background document C), all these documents are also considered to be part of this review report.

2. Purposes of this review report

This review report, including the background documents and appendices thereto, has been developed in support of the Commission Implementing **Regulation (EU) No 563/2014[4]** concerning the approval of *Chitosan Hydrochloride* as basic substance under Regulation (EC) No 1107/2009.

The review report will be made available for public consultation by any interested parties.

Without prejudice to the provisions of Regulation (EC) No 178/2002[5], in particular with respect to the responsibility of operators, following the approval of *Chitosan Hydrochloride* as basic substance, operators are responsible for using it for plant protection purposes in conformity with the legal provisions of Regulation (EC) No 1107/2009 and with the conditions established in the sections 4, 5 and Appendixes I and II of this review report.

EFSA will make available to the public all background documents and the final Technical Report of EFSA, as well as the application without the Appendixes and excluding any information for which confidential treatment is justified in accordance with the provisions of Article 63 of Regulation (EC) No 1107/2009.

Products containing exclusively one or more basic substances do not require authorisation in line with derogation set under Article 28 of Regulation (EC) No 1107/2009. As a consequence, no further assessment will be carried out on such products. However, the Commission may review the approval of a basic substance at any time in conformity with the provisions of Article 23(6) of Regulation (EC) No 1107/2009.

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[3] European Food Safety Authority, 2013; Outcome of the consultation with Member States and EFSA on the basic substance application for chitosan hydrochloride and the conclusions drawn by EFSA on the specific points raised. EFSA supporting publication 2013:EN-426. 39 pp.

[4] OJ L 156, 24.05.2014, p. 5–7.

[5] OJ L 31, 1.2.2002 p. 1-24 - Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety.

3. Overall conclusion in the context of Regulation (EC) No 1107/2009

The overall conclusion based on the application, including the results of the evaluation carried out with the scientific assistance of EFSA, and the comments and further additional information provided by the applicant to address the open points identified in the Technical report from EFSA, is that there are clear indications that it may be expected that *Chitosan Hydrochloride* fulfils the criteria of Article 23.

The term Chitosan refers to several derivatives which differ with regard to their chemical and physical properties but are made up of glucosamine monomers. Chitosan derivatives are used in medicine, food and cosmetics.

Glucosamine is one of the most abundant mono-saccharides in nature. It is part of the structure of chitin, which composes the exoskeleton of crustaceans and other arthropods, as well as the cell walls of several fungi.

Chitin is a long chain polymer of N-acetyl- glucosamine and is abundantly occurring in nature. Fungal chitin has several forms and is also related to the species of edible fungi.

The form chitin-glucan from *Aspergillus niger* was authorised as novel food ingredient by the Commission Decision 2011/76/EU authorising the placing on the market of a chitin-glucan ingredient under Regulation (EC) No 258/97 of the EU Parliament and Council[6]. The decision was based on the EFSA scientific opinion of the Panel on Dietetic Products, Nutrition and allergies[7] which reports safe use under the proposed conditions of use and levels of intake (maximum dose of 5 g per day).

Specifications reported in the Commission Decision 2011/76/EU refers to chitin-glucan composed of two polysaccharides: chitin composed of repeating units of N-acetyl –D-glucosamine (CAS No 1398-61-4) and beta (1,3) glucan composed of repeating units of D-glucose (CAS No 9041-22-9). Moreover, in chapter 8.5 of the EFSA scientific opinion "the polysaccharides related to chitin-glucan and on which toxicological data are available are chitin (of crustacean origin), chitosan (derived from chitin of crustacean origin), beta-glucan (of vegetable and fungal origin) and oligomers of chitosan. No safety concern arises from these data."

In addition, the form glucosamine-hydrochloride has been subject to a scientific opinion of the EFSA Panel on Dietetic Products, Nutrition and allergies of the safety of glucosamine hydrochloride from *Aspergillus niger* as food ingredient in the context of Regulation (EC) No 258/97 on novel food. The Panel therein concluded on the safety of the product as food ingredient for adult consumers at the proposed intake of 750 mg of glucosamine per day[8]. As reported in that EFSA scientific opinion: "The toxicity of glucosamine has been studied in a number of animal species. Glucosamine has a very low acute oral toxicity. …The Panel considers that glucosamine has also a low chronic toxicity"[9].

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6 OJ L 29, 3.2.2011, p.34-35.

7 EFSA Journal (2010) 8(7):1687.

8 EFSA Journal (2009) 1099:1-19.

9 EFSA Journal (2009) 1099:1-19.

The form Chitosan has been subject to an EFSA opinion on the substantiation of health claims[10] related to chitosan effecting maintenance of normal blood LDL-cholesterol concentrations with positive results, leading to the inclusion of chitosan into the Commission Regulation (EC) 432/2012 establishing a list of permitted health claims made on foodstuffs[11], where the recommended use is 3 g of chitosan as daily intake for adult.

The food grade specifications refer to Chitosan as a polymer composed of ß-(1-4) linked D-glucosamine and N-acetyl-D-glucosamine.

The characterisation of chitosan in that opinion was "Chitosan is a linear cationic polysaccharide composed of randomly distributed ß-(1-4)-linked D-glucosamine and N-acetyl-D-glucosamine produced commercially by the de-acetylation of chitin, which is a component of the exoskeleton of crustaceans and the cell walls of fungi. The degree of de-acetylation can be measured by established methods, and ranges from 60-100 % in commercial preparations. The molecular weight of chitosan in commercial preparations ranges from 3,800 to 20,000 Da. Chitosan is insoluble in water.

The Panel considers that the food constituent, chitosan, which is the subject of the health claims, is sufficiently characterised."

Chitosan Hydrochloride which is subject to the current application as basic substance, is produced by the de-acetylation of chitin (crustaceans cells) and salinization using hydrochloric acid to result in the form of hydrochloride in order to enhance its solubility in water . The molecular weight in this form ranges from 47.000 to 65.000 Da [12].

Considering the EFSA conclusions on the basic substance application for Chitosan Hydrochloride, the opinions of the EFSA Panel on Dietetic Products, Nutrition and allergies on chitosan and derivatives, the rate of application and the conditions of use which are described in detail in Appendix I and II, it is concluded that the use of chitosan hydrochloride would not lead to concerns for human health. Furthermore, no residues are expected as the conditions of use would not significantly increase the background level due to the natural occurrence of the substance.

Chitosan Hydrochloride is not a substance of concern and does not have an inherent capacity to cause endocrine disrupting, neurotoxic or immune-toxic effects and is not predominantly used for plant protection purposes but nevertheless is useful in plant protection in a product consisting of the substance and water. Finally, it is not placed on the market as a plant protection product.

It can be concluded that the substance has neither an immediate or delayed harmful effect on human or animal health nor an unacceptable effect on the environment when used in accordance with the supported uses as described in Appendix II.

In fact, these indications were reached within the framework of the uses which were supported by the applicant and mentioned in the list of uses supported by available data (attached as

[10] EFSA Journal (2011); 9(6):2214

[11] OJ, L 136, 25.5.2012, p.1

[12] Outcome of the consultation with member States and EFSA on the basic substance application for *Chitosan Hydrochloride* and the conclusions drawn by EFSA on the specific points raised. 2013:EN-NNNN.39 pp.

Appendix II to this review report) and therefore, they are also subject to compliance with the particular conditions and restrictions in sections 4 and 5 of this report.

Extension of the use pattern beyond those described above will require an evaluation at Community level in order to establish whether the proposed extensions of use can still satisfy the requirements of Article 23 of Regulation (EC) No 1107/2009.

4. Identity and biological properties

The main properties of *Chitosan Hydrochloride* are given in Appendix I.

Chitosan Hydrochloride of animal origin must be in compliance with Regulation (EC) No 1069/2009 and Regulation (EU) No 142/2011.

Specifications laid down in the European Pharmacopeia must be complied with.

It has been established that for *Chitosan Hydrochloride* as notified by the applicant, the following manufacturing impurities are considered, on the basis of information currently available, of toxicological or environmental concern:

Heavy metals: Maximum level of 40 ppm.

5. Particular conditions to be taken into account in relation to the uses as basic substance of Chitosan Hydrochloride

Chitosan Hydrochloride must be identified by the specifications given in Appendix I and must be used in compliance with conditions of supported uses as reported in Appendixes I and II.

The following conditions for use deriving from assessment of the application have to be respected by users:

- Only uses as basic substance being elicitor of the crop's self-defence mechanisms are approved.

Use of chitosan hydrochloride must be in compliance with conditions specified in the Appendixes I and II of this review report and the Maximum application rate of chitosan hydrochloride for a single treatment is: 800 gr/ha.

On the basis of the proposed and supported uses (as listed in Appendix II), no particular issues have been identified.

The identification of Chitosan as food ingredient implies that the Regulation (EC) No 178/2002 on food safety applies and consequently this includes the respect to any maximum permissible levels of chemical and biological contaminants legally set for this type of product.

6. List of studies to be generated

No further studies were identified which were at this stage considered necessary.

7. Updating of this review report

The information in this report may require to be updated from time to time to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 23 of Regulation (EC) No 1107/2009. Any such adaptation will be finalised in the Standing Committee on the Food Chain and Animal Health, as appropriate, in connection with any amendment of the approval conditions for *Chitosan hydrochloride* in Part C of Annex of the Regulation (EC) No 540/2011.

8. Recommended disclosure of this review report

Considering the importance of the respect of the approved conditions of use and the fact that a basic substance will be not placed on the market as plant protection product, hence, no further assessment will have to be carried out on it, it is very important to inform not only applicants but also potential users on the existence of this review report.

It is therefore recommended that the competent authorities of Member States will make available such report to general public and operators by means of their national relevant websites and by any other appropriate form of communication to ensure that the information reaches potential users.

APPENDIX I

Identity and biological properties

CHITOSAN HYDROCHLORIDE

Common name (ISO)	Not relevant
Chemical name (IUPAC)	Not relevant
Chemical Name. (CA)	Not relevant
Common names	Chitosan Linear polysaccharide composed of randomly distributed 1-4 linked D glucosamine and N-acetyl-D-glucosamine produced by de-acetylation of chitin. The use of hydrochloric acid to create the form hydrochloride is to increase solubility in water.
CAS No	9012-76-4
CIPAC No and EEC No	Not relevant
FAO SPECIFICATION	Not relevant
Minimum purity	European Pharmacopeia Chitosan being a product of animal origin must be in compliance with the requirements of Regulation (EC) No 1069/2009 and Commission Regulation (EU) No 142/2011.
Molecular formula	Not relevant
Relevant impurities	Max content of heavy metals: 40 ppm
Molecular mass and structural formula	Not relevant
Mode of Use	Chitosan hydrochloride as specified above to be used in water solution for application on various crops or for seed treatment.
Preparation to be used	Chitosan hydrochloride to be diluted in compliance with rate of application reported in Appendix II.
Function of plant protection	Elicitor, having a fungicide and bactericide effect via the stimulation of natural defence mechanisms.

APPENDIX II

CHITOSAN HYDROCHLORIDE

Crop and/ or situation (a)	**Member State or Country**	**Example product of Chitosan hydrochloride. as available on the market**	**F G or I** (b)	**Pests or group of pests controlled** (c)	**Formulation**		**Application of chitosan hydrochloride**				**Application rate of chitosan hydrochloride**			**PHI** (days) (m)	**Remarks***
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage & season (j)	No. of application min/max (k)	Interval between applications (min)	a.i./hl min max (g/hl)	Water l/ha min max	Total rate each application g a.i./ha min max (g/ha) (l)		
Fruits berries and small fruit	All	Chitoplant	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	Low-Medium volume spraying	From 1 Leaf development (main shoot) to 7 Development of fruit	4-8	Two weeks	50 - 200	200 - 400	100-800	0	
Vegetables	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	Low-Medium volume spraying	From 1 Leaf development (main shoot) to 7 Development of fruit	4-8	Two weeks	50 - 100	200 - 400	100-400	0	

List of uses supported by available data

Crop and/ or situation (a)	**Member State or Country**	**Example product of Chitosan hydrochloride. as available on the market**	**F G or I** (b)	**Pests or group of pests controlled** (c)	**Formulation**		**Application of chitosan hydrochloride**				**Application rate of chitosan hydrochloride**			**PHI** (days) (m)	**Remarks***
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage & season (j)	No. of application min/max (k)	Interval between applications (min)	a.i./hl min max (g/hl)	Water l/ha min max	Total rate each application g a.i./ha min max (g/ha) (l)		
Cereals	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	Low-Medium volume spraying	From 1 Leaf development (main shoot) to 7 Development of fruit	4 - 8	2 week	50 - 100	200 - 400	100-400	0	
Spices	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	Low-Medium volume spraying	From 1 Leaf development (main shoot) to 7 Development of fruit	4 - 8	2 week	50 - 100	200 - 400	100-400	0	

List of uses supported by available data

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					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage & season (j)	No. of application min/max (k)	Interval between applications (min)	a.i./hl min max (g/hl)	Water l/ha min max	Total rate each application g a.i./ha min max (g/ha) (l)		
Crops for animal feed	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	Low-Medium volume spraying	From 1 Leaf development (main shoot) to 7 Development of fruit	4 - 8	2 week	50 - 100	200 - 400	100-400	0	
Cereals *Seed treatment*	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	low volume spraying.	Before sowing	1	Not applicable	50 - 100	Not applicable	Not applicable	0	
Potatoes *Seed treatment*	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	low volume spraying/ dipping	Before sowing	1	Not applicable	50 - 100	Not applicable	Not applicable	0	

List of uses supported by available data

Crop and/ or situation (a)	**Member State or Country**	**Example product of Chitosan hydrochloride. as available on the market**	**F G or I** (b)	**Pests or group of pests controlled** (c)	**Formulation**		**Application of chitosan hydrochloride**				**Application rate of chitosan hydrochloride**			**PHI** (days) (m)	**Remarks***
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage & season (j)	No. of application min/max (k)	Interval between applications (min)	a.i./hl min max (g/hl)	Water l/ha min max	Total rate each application g a.i./ha min max (g/ha) (l)		
Sugar beet Seed treatment	All	*ChitoPlant*	F G	*Plant elicitor, plant resistance against pathogenic fungi and bacteria*	*SP Soluble powder*	*100% chitosan hydrochloride*	low volume spraying/ dipping	Before sowing	1	Not applicable	50 - 200	Not applicable	Not applicable	0	

* For uses where the column „Remarks. As above or other conditions to take into account	(i) g/kg or g/L. Normally the rate should be given for the substance (according to ISO)
(a) For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)	(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)	(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(c) *e.g.* pests as biting and suckling insects, soil born insects, foliar fungi, weeds or plant elicitor	(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) etc..	(m) PHI - minimum pre-harvest interval
(e) GCPF Codes – GIFAP Technical Monograph N° 2, 1989	
(f) All abbreviations used must be explained	
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench	
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant – type of equipment used must be indicated	