## CONCLUSION ON PESTICIDE PEER REVIEW

# Conclusion on the peer review of the pesticide risk assessment of the active substance COS-OGA[1]

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## ABSTRACT

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State Belgium for the pesticide active substance COS-OGA are reported. The context of the peer review was that required by Regulation (EC) No 1107/2009 of the European Parliament and of the Council. The conclusions were reached on the basis of the evaluation of the representative use of COS-OGA as an elicitor to control powdery mildew (*Sphaerotheca fuliginea*) on cucurbits grown under glasshouses. An application for inclusion of COS-OGA in Annex IV of Regulation (EC) No 396/2005 was assessed. The reliable endpoints concluded as being appropriate for use in regulatory risk assessment derived from the available studies and literature in the dossier peer reviewed, are presented. Missing information identified as being required by the regulatory framework is listed.



## KEY WORDS

COS-OGA, peer review, risk assessment, pesticide, elicitor

[1] On request from the European Commission, Question No EFSA-Q-2014-00014, approved on 1 October 2014. It is noted that the IUPAC name that corresponds to the company's code COS-OGA is: Linear copolymer of $\alpha$-1,4-*D*-galactopyranosyluronic acids and methylesterified galactopyranosyluronic acids (9 to 20 residues) with linear copolymer $\beta$-1,4-linked 2-amino-2-deoxy-*D*-glucopyranose and 2-acetamido-2-deoxy-*D*-glucopyranose (5 to 10 residues).

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## SUMMARY

COS-OGA is a new active substance for which in accordance with Article 7 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council (hereinafter referred to as 'the Regulation'), the rapporteur Member State (RMS) Belgium received an application from FytoFend S.A. on 28 June 2012 for approval. In accordance with Article 8(1)(g) of the Regulation, FytoFend S.A. submitted an application for inclusion of the active substance into Annex IV of Regulation (EC) No 396/2005. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 5 December 2012.

The RMS provided its initial evaluation of the dossier on COS-OGA in the Draft Assessment Report (DAR), which was received by the EFSA on 19 December 2013. The peer review was initiated on 14 January 2014 by dispatching the DAR for consultation of the Member States and the applicant FytoFend S.A.

Following consideration of the comments received on the DAR, it was concluded that additional information should be requested from the applicant and that there was no need to conduct an expert consultation.

In accordance with Article 12 of the Regulation, the EFSA should adopt a conclusion on whether COS-OGA can be expected to meet the approval criteria provided for in Article 4 of the Regulation taking into consideration recital (10) of the Regulation and give a reasoned opinion concerning the Annex IV proposal as referred to in Article 10(1) of Regulation (EC) No 396/2005.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative use of COS-OGA as an elicitor to control powdery mildew (*Sphaerotheca fuliginea*) on cucurbits grown in glasshouses, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

When applied on cucumber according to the proposed GAP against powdery mildew, the efficacy of COS-OGA was seen to be similar to the chemical references in case of low disease pressure.

A data gap was identified for a search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side-effects on the environment and non-target species

In the section on identity, physical/chemical/technical properties and methods of analysis a data gap was identified in relation to the methods of analysis for the environment.

In the section on mammalian toxicology no data gaps or critical areas of concern were identified.

In the section on residues no data gaps or critical areas of concern were identified.

It is proposed to include COS-OGA in Annex IV of Regulation (EC) No 396/2005.

A data gap was identified for a readily biodegradation study. In the absence of this study COS-OGA should be considered as not readily biodegradable. Due to the nature of the substance and to the fact that the representative use proposed is restricted to greenhouse no further assessment is deemed necessary to address the risk to soil organisms and groundwater.

In the section on ecotoxicology a data gap was identified to provide the mandatory toxicity studies on aquatic organisms.

## TABLE OF CONTENTS

## BACKGROUND

Regulation (EC) No 1107/2009 of the European Parliament and of the Council[3] (hereinafter referred to as 'the Regulation') lays down, *inter alia*, the detailed rules as regards the procedure and conditions for approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant(s) for comments on the initial evaluation in the Draft Assessment Report (DAR) provided by the rapporteur Member State (RMS) and co-rapporteur Member State (co-RMS FR), and the organisation of an expert consultation where appropriate.

In accordance with Article 12 of the Regulation, EFSA is required to adopt a conclusion on whether an active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation (also taking into consideration recital (10) of the Regulation) within 120 days from the end of the period provided for the submission of written comments, subject to an extension of 30 days where an expert consultation is necessary, and a further extension of up to 150 days where additional information is required to be submitted by the applicant(s) in accordance with Article 12(3).

COS-OGA is a new active substance for which in accordance with Article 7 of the Regulation, the rapporteur Member State (RMS) Belgium (hereinafter referred to as the 'RMS') received an application from FytoFend S.A. on 28 June 2012 for approval of the active substance COS-OGA. In accordance with Article 8(1)(g) of the Regulation, FytoFend S.A. submitted an application for inclusion of COS-OGA into Annex IV of Regulation (EC) No 396/2005.[4] Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 5 December 2012.

The RMS provided its initial evaluation of the dossier on COS-OGA in the Draft Assessment Report (DAR), which was received by the EFSA on 19 December 2013 (Belgium, 2013). The DAR included a proposal to include COS-OGA into Annex IV of Regulation (EC) No 396/2005. The peer review was initiated on 14 January 2014 by dispatching the DAR for consultation of the Member States and the applicant FytoFend S.A. for consultation and comments. EFSA also provided comments. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 12(3) of the Regulation were considered in a telephone conference between the EFSA, the RMS, the co-RMS, and the European Commission on 7 May 2014. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof it was concluded that additional information should be requested from the applicant and that there was no need to conduct an expert consultation.

The outcome of the telephone conference, together with the EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, were reported in the final column of the Evaluation Table.

[3] Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1-50.

[4] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1-16.

In accordance with Article 12 of the Regulation, the EFSA should adopt a conclusion on whether COS-OGA can be expected to meet the approval criteria provided for in Article 4 of the Regulation taking into consideration recital (10) of the Regulation and give a reasoned opinion concerning the Annex IV proposal as referred to in Article 10(1) of Regulation (EC) No 396/2005. A final consultation on the conclusions arising from the peer review of the risk assessment and on the MRL application took place with Member States via a written procedure in September 2014.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative use of COS-OGA as an elicitor to control powdery mildew (*Sphaerotheca fuliginea*) on cucurbits grown in glasshouses. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A.

In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2014) comprises the following documents, in which all views expressed during the course of the peer review, including minority views where applicable, can be found:

- the comments received on the DAR,
- the Reporting Table (13 May 2014),
- the Evaluation Table (30 September 2014),
- the comments received on the assessment of the additional information (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its final addendum (compiled version of September 2014 containing all individually submitted addenda (Belgium, 2014)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated to have regulatory access to the information on which this conclusion report is based.

## THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

COS (Chito-OligoSaccharides) -OGA (Oligo-Galacturonic Acid) consists of an oligosaccharide complex composed of a polyanionic structure stabilized by one polycationic chain. The IUPAC name is Linear copolymer of $\alpha$-1,4-*D*-galactopyranosyluronic acids and methylesterified galactopyranosyluronic acids (9 to 20 residues) with linear copolymer $\beta$-1,4-linked 2-amino-2-deoxy-*D*-glucopyranose and 2-acetamido-2-deoxy-*D*-glucopyranose (5 to 10 residues) the company code is COS-OGA. COS is also known as chitosan and OGA is derived from pectin. There is no ISO common name for this active substance.

The representative formulated product for the evaluation was 'FYTO11' a soluble concentrate containing 12.5 g/l of the complex.

The representative use evaluated comprises glasshouse foliar spraying against foliar fungi. The complex is not a fungicide, it elicits the plants natural defences. Full details of the GAP can be found in the list of end points in Appendix A.

The recommendations of the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013) have been considered for the assessment of the effectiveness of the active substance. A total of three efficacy trials conducted on cucumber against powdery mildew (*Sphaerotheca fuliginea*) in the EU under glasshouse conditions were reported. When applied according to the proposed GAP, the efficacy was seen to be similar to the chemical references in two trials with low disease pressure, but lower in one trial where the severity of the disease was more important.

## CONCLUSIONS OF THE EVALUATION

### 1. Identity, physical/chemical/technical properties and methods of analysis

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 rev.4 (European Commission, 2000), SANCO/10597/2003 – rev. 10.1 (European Commission, 2012), and SANCO/825/00 rev. 8.1 (European Commission, 2010).

The material as manufactured contains 915 g/kg with OGA/COS ratio of between 1-1.6, DP (degree of polymerisation) of COS between 5-10, DP of OGA between 9-20, DM (degree of methylation) of OGA < 10%, DA (degree of acetylation) of COS < 50%. The technical material contains no relevant impurities.

No information was given on the level of microbial contamination and the mechanism for the control of such contamination and its possible increase on storage.

The main data regarding the identity of the complex and its physical and chemical properties are given in Appendix A.

Methods of analysis are available for the technical material and the formulation.

Methods for residues in plants and animals are not required (see section 3). The residue definition for monitoring in the environment has been identified to be the COS-OGA. As a result methods of analysis for the environment have been identified as a data gap.

The active substance is not classified as a Health Hazard under GHS and therefore a method of analysis is not required for body fluids and tissues.

### 2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000 rev. 10 - final (European Commission, 2003), SANCO/10597/2003 – rev. 10.1 (European Commission, 2012) and Guidance on Dermal Absorption (EFSA PPR Panel, 2012).

The COS-OGA complex has a high molecular weight. Under physiological conditions, the complex mostly dissociates and therefore, it was considered appropriate to study the COS and OGA components separately. COS is obtained from hydrolysis of chitosan and OGA is obtained from pectin. Both compounds are abundant in nature and humans are commonly exposed to them. No relevant impurities were identified in the technical specification.

Chitosan is proposed as excipient in preparations for inhalation formulations to increase bioavailability of drugs at the nasal mucosa and in the lungs, its constituents, *N*-acetylglucosamine and glucosamine are present and synthesised in all living organisms including humans. Pectin is consumed mostly in the form of fruits and vegetables but also as hydrocolloid in "functional foods", jellies and milk products. Important published literature exists on pectin and to a lesser extent on chitosan. No adverse effects were seen in the available toxicity studies. Overall no toxicological concern was identified on the components of COS-OGA and therefore no reference values were set and an operator, worker, bystander and residential exposure risk assessment were considered unnecessary.

## 3. Residues

In the absence of the need for toxicological reference values for COS-OGA the investigation of residues and consumer exposure estimates are not necessary and therefore, EFSA is of the opinion that the setting of MRLs is not necessary and that the inclusion of COS-OGA in Annex IV of Regulation (EC) No 396/2005 might be appropriate.

## 4. Environmental fate and behaviour

A search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with environmental fate of COS OGA components and published within the last 10 years before the date of submission of dossier was done by the applicant. However, this was not done in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

The applicant claims, based on theoretical considerations, that the two components of COS-OGA: chitosan (COS) and pectin (OGA) form a complex within the pH range 3.6 – 6.5, which would be responsible of the fungicidal activity attributed to the substance. No study has been submitted to demonstrate the actual existence of this complex and /or its stability under normal environmental conditions. No studies on the degradation of COS-OGA and its components in the different environmental compartments are available. A number of studies published in scientific journals are presented. These studies show that chitin, chitosan and pectin can be degraded by different species of microbes. However, from the information in these studies it is not possible to estimate the persistence of the complex and its components under natural environmental conditions in European agricultural areas. Also it is not possible to know if the formation of the complex can affect the rate of degradation of its components.

Hydrolysis and aqueous photolysis studies of COS-OGA and of its components are not available. Taking into account their chemical structure, they may be expected to be stable to hydrolysis and photolysis under normal environmental conditions. No readily biodegradation study is available for COS-OGA and a data gap has been identified. In absence of reliable readily biodegradation study the substance would need to be considered as not readily biodegradable.

Due to the nature of the substance and to the fact that the representative use proposed is restricted to greenhouse no further assessment is deemed necessary to address the risk to soil organisms and groundwater. The RMS calculated worst case initial PEC SW values of 0.21 µg /L based on the representative use in greenhouses (FOCUS, 2008). This PEC is used to perform the risk assessment for the aquatic environment.

## 5. Ecotoxicology

A search of the scientific peer-reviewed open literature relevant to the scope of the application, dealing with side-effects on non-target species and published within the last 10 years before the date of submission of dossier was done by the applicant. However, this was not done in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011). In addition, the literature search was not considered exhaustive since it covered only birds and fish.

Taking into account the representative use of COS-OGA to control mildew on cucurbits under permanent greenhouse, the exposure to birds and mammals was considered negligible. Therefore, the risk to birds and mammals was considered as low.

No toxicity studies were available for COS-OGA on aquatic organisms except an early-life stage (ELS) test with fish. However, the maintenance of the test item concentration in water in this study was not confirmed; therefore it could not be considered as valid. Studies from the literature were also submitted showing the digestive chitinolytic activity in fish, the presence in the tissues of fish of a number of enzymes (chitinases, chitobiases and lysozymes) able to degrade chitin and chitosan and the improvement in growth, survival and immune response in fish administered with chitosan. Although further information would be needed to address the hazard characterisation for aquatic organisms (data gap), particularly for invertebrates and algae, the risk could be considered as low for the representative use in greenhouse, based on a weight of evidence approach (e.g. nature of the substance and relatively low exposure).

Based on the available data the risk to bees was concluded as low. For non-target arthropods other than bees, two toxicity studies were available, one with *Typhlodromus pyri* and another with *Aphidius rhopalosiphi* and *Episyrphus balteatus*.. However, it is unclear whether the tested concentrations in the study with the two latter species cover the representative use as reported in the GAP. Considering the representative use in permanent glasshouses, a low risk to non target arthropods was concluded.

Based on the representative use in permanent glasshouses, the expected degradation of COS-OGA in the environment due to the action of many enzymes secreted by a number of microorganisms and the amount of COS and OGA being minor compared to their background level, the exposure to soil organisms is considered negligible. Therefore, toxicity studies with soil organisms, including soil microorganisms, non target terrestrial plants and organisms involved in biological methods for sewage treatment were considered not relevant to conclude on a low risk.

## 6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

### 6.1. Soil

| Compound (name and/or code) | Persistence | Ecotoxicology |
|---|---|---|
| COS-OGA | No data. | Low risk to soil dwelling organisms |
| COS (chitosan) | No data | Low risk to soil dwelling organisms |
| OGA (hydrolysis derivative of pectin) | No data | Low risk to soil dwelling organisms |

### 6.2. Groundwater

| Compound (name and/or code) | Mobility in soil | >0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter) | Pesticidal activity | Toxicological relevance | Ecotoxicological activity |
|---|---|---|---|---|---|
| COS-OGA | No data available | No data available | No | No | Low risk to organisms living in surface water for representative use assessed |
| COS (chitosan) | No data available | No data available | No | No | Low risk to organisms living in surface water for representative use assessed |
| OGA (hydrolysis derivative of pectin) | No data available | No data available | No | No | Low risk to organisms living in surface water for representative use assessed |

### 6.3. Surface water and sediment

| **Compound (name and/or code)** | **Ecotoxicology** |
|---|---|
| COS-OGA | Low risk to organisms living in surface water |
| COS (chitosan) | Low risk to organisms living in surface water |
| OGA (hydrolysis derivative of pectin) | Low risk to organisms living in surface water |

### 6.4. Air

| **Compound (name and/or code)** | **Toxicology** |
|---|---|
| COS-OGA | No toxicological concern |

## 7. Data gaps

This is a list of data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of the Regulation concerning information on potentially harmful effects).

- Methods of analysis for the environment (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown, see section 1).

- A search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side-effects on the environment and non-target species and published within the last 10 years before the date of submission of dossier, to be conducted and reported in accordance with the Guidance of EFSA on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for all representative uses evaluated; submission date proposed by the applicant: unknown, see sections 4, 5).

- OECD 301 Readily biodegradability test needs to be provided for COS-OGA and its components chitosan and pectin (relevant for all representative uses evaluated; no submission date proposed by the applicant: unknown, see section 4).

- The mandatory toxicity studies with aquatic organisms (acute toxicity test for fish, acute toxicity test for aquatic invertebrates and chronic study for algae) should be provided (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

## 8. Particular conditions proposed to be taken into account to manage the risk(s) identified

No particular conditions are proposed for the representative uses evaluated.

## 9. Concerns

### 9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011[5] and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as an issue that could not be finalised where the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation.

- Issues that could not be finalised were not identified for the representative use assessed.

### 9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

[5] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127-175.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where in the light of current scientific and technical knowledge using guidance documents available at the time of application the active substance is not expected to meet the approval criteria provided for in Article 4 of the Regulation.

- Critical areas of concern were not identified for the representative use assessed.

### 9.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

| **Representative use** | | **Cucurbits (glasshouse)** |
|---|---|---|
| **Operator risk** | Risk identified | |
| | Assessment not finalised | |
| **Worker risk** | Risk identified | |
| | Assessment not finalised | |
| **Bystander risk** | Risk identified | |
| | Assessment not finalised | |
| **Consumer risk** | Risk identified | |
| | Assessment not finalised | |
| **Risk to wild non target terrestrial vertebrates** | Risk identified | |
| | Assessment not finalised | |
| **Risk to wild non target terrestrial organisms other than vertebrates** | Risk identified | |
| | Assessment not finalised | |
| **Risk to aquatic organisms** | Risk identified | |
| | Assessment not finalised | |
| **Groundwater exposure active substance** | Legal parametric value breached | |
| | Assessment not finalised | |
| **Groundwater exposure metabolites** | Legal parametric value breached[(a)] | |
| | Parametric value of 10µg/L[(b)] breached | |
| | Assessment not finalised | |
| **Comments/Remarks** | | |

The superscript numbers in this table relate to the numbered points indicated in Sections 9.1 and 9.2. Where there is no superscript number see Sections 2 to 6 for further information.

(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December.
(b): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003.

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# APPENDICES

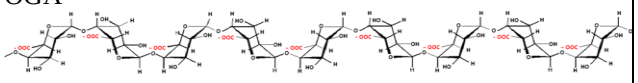
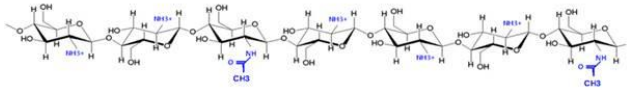
## APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

### Identity, Physical and Chemical Properties, Details of Uses, Further Information

| | |
|---|---|
| Active substance (ISO Common Name) ‡ | No ISO common name;<br>Oligosaccharidic complex comprising oligopectates and chitooligosaccharides<br>(code: COS-OGA) |
| Function (*e.g.* fungicide) | Elicitor |
| Rapporteur Member State | Belgium |
| Co-Rapporteur Member State | France |

**Identity** (Annex IIA, point 1)

| | |
|---|---|
| Chemical name (IUPAC) ‡ | Linear copolymer of α-1,4-D-galactopyranosyluronic acids and methylesterified galactopyranosyluronic acids (9 to 20 residues) with linear copolymer β-1,4-linked 2-amino-2-deoxy-D-glucopyranose and 2-acetamido-2-deoxy-D-glucopyranose (5 to 10 residues) |
| Chemical name (CA) ‡ | - |
| CIPAC No ‡ | - |
| CAS No ‡ | - |
| EEC No (EINECS or ELINCS) ‡ | - |
| FAO Specification (including year of publication)‡ | - |
| Minimum purity of the active substance as manufactured (g/kg) ‡ | Minimum purity is 915 g/kg with:<br>- OGA/COS ratio comprised between 1-1.6<br>- DP (degree of polymerisation) of COS comprised between 5-10<br>- DP of OGA comprised between 9-20<br>- DM (degree of methylation) of OGA < 10%<br>- DA (degree of acetylation) of COS < 50%<br><br>(N.B. Based on pilot scale production) |
| Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg) | None |
| Molecular formula ‡ | OGA:<br>HO-[C6H8O6](9-20)-H with DM <10 (max 10% HO-[C7H10O6](9-20)-H)<br><br>COS:<br>HO-[C8H13NO5](5-10)-H with DA < 50% (max 50% HO-[C6H11NO4](5-10)-H) |

| | |
|---|---|
| Molecular mass ‡ | OGA: 1726 g/mol (based on mean DP of 11 and mean DM 8.6%) [1690 g/mol*0.914 + 2108 g/mol*0.086)]<br><br>COS: 1243 g/mol (based on mean DP of 7 and mean DA 21%) [1299 g/mol*0.79 + 1033 g/mol*0.21)] |
| Structural formula ‡ | OGA<br>  <br>+<br>COS (partially acetylated)<br>  |

## Physical-chemical properties (Annex IIA, point 2)

| | |
|---|---|
| Melting point (state purity) ‡ | Not determined. See Temperature of decomposition. |
| Boiling point (state purity) ‡ | Not determined. See Temperature of decomposition. |
| Temperature of decomposition | Not determined.<br><br>A decrease of around 50 % of the molecular weight of pectate is observed after 50 minutes at 95°C.<br><br>The initial decomposition temperature of chitosan is 254.6°C whereas the main decomposition temperature is around 296.3°C |
| Appearance (state purity) ‡ | Homogeneous beige liquid with a gelatinous aspect |
| Vapour pressure (in Pa, state temperature) ‡ | Not determined. Not relevant due to the similar nature and structure with sucrose which is a non-volatile compound |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) ‡ | Not determined. See above vapour pressure |
| Solubility in water (g/l or mg/l, state temperature) ‡ | Cannot be determined. COS-OGA is already solubilized at 24.5g/L |
| Solubility in organic solvents (in g/l or mg/l, state temperature) ‡ | n-heptane: <100 mg/l (20°C)<br>1,2-dichloroethane: <100 mg/l (20°C)<br>methanol: <100 mg/l (20°C)<br>acetone: <100 mg/l (20°C)<br>ethyl acetate: <100 mg/l (20°C) |
| Surface tension‡ | 51.5 mN/m (1g/L, 20°C) |
| Partition co-efficient (log $P_{OW}$) (state pH and temperature) ‡ | Cannot be determined. COS-OGA is already solubilized at 24.5 g/L |
| Dissociation constant ‡ | Not determined |
| UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) ‡ | No maximum of absorbance in acid, basic or neutral conditions |
| Flammability ‡ | Not determined. Not relevant taking into account the nature of the active substance. Not flammable |
| Explosive properties ‡ | Not determined. Not relevant taking into account the nature of the active substance. Not explosive |
| Oxidizing properties ‡ | Not determined. Not relevant taking into account the nature of the active substance. Not oxidizing |

## Summary of representative uses evaluated (COS-OGA)

| Crop and/ or situation (a) | Zone | Product code | F G or I (b) | Pests or Group of pests controlled (c) | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) (l) | Remarks: (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Type (d-f) | Conc. of as (i) | method kind (f-h) | growth stage & season (j) | number min-max (k) | interval between applications (min) | kg as/hL min-max | water L/ha min-max | kg as/ha min max | | |
| Cucurbits under greenhouse | EU | FYTO11 | G | Foliar fungi | Soluble concentrated (SL) | 12.5 g/L | Foliar spraying | BBCH 13 to BBCH 73 | 5 | 7 days | 0.005 | 500 L/ha Leaf Wall Area | 0.025 kg as/ha Leaf Wall Area Or 0.063 kg a.s./ha soil | 0 day | / |

Remarks :

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (eg. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) eg. biting and sucking insects, soil bourne insects, foliar fungi, weeds
(d) eg. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, eg. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, eg. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated g/kg or g/l[6]
(i) 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
(j) The minimum and maximum number of applications possible under practical conditions of use must be provided
(k) PHI - minimum pre-harvest interval
(l) Remarks may include: Extent of use/economic importance/restrictions

[6] The application rate of 0.025 kg a.s./ha Leaf Wall Area (LWA) is equivalent to 0.063 kg a.s./ha soil, assuming a distance between rows of 1.6 m and a treated height of plants of 2 m

## Further information, Efficacy

**Effectiveness (Regulation (EU) N° 284/2013, Annex Part A, point 6.2)**

| |
|---|
| When applied according to the representative GAP (5x 0.025 kg a.s./ha LWA) against powdery mildew on cucumber:<br>- Similar efficacy to the chemical reference in case of low disease pressure.<br>- lower efficacy (34%) compared to the chemical reference (86%) in case of important disease pressure. |

**Adverse effects on field crops (Regulation (EU) N° 284/2013, Annex Part A, point 6.4)**

| |
|---|
| No adverse effects reported |

**Observations on other undesirable or unintended side-effects (Regulation (EU) N° 284/2013, Annex Part A, point 6.5)**

| |
|---|
| No undesirable effect reported |

**Groundwater metabolites: Screening for biological activity (SANCO/221/2000-rev.10-final Step 3 Stage 1)**

| |
|---|
| Not relevant |

## Methods of Analysis

### Analytical methods for the active substance (Annex IIA, point 4.1)

| | |
|---|---|
| Technical as (principle of method) | Spectrophotometric (colorimetric) method |
| Impurities in technical as (principle of method) | Atomic absorption spectrophotometry. |
| Plant protection product (principle of method) | Spectrophotometric (colorimetric) method. |

### Analytical methods for residues (Annex IIA, point 4.2)

### Residue definitions for monitoring purposes

| | | |
|---|---|---|
| Food of plant origin | | None |
| Food of animal origin | | None |
| Soil | | COS-OGA |
| Water | surface | COS-OGA |
| | drinking/ground | COS-OGA |
| Air | | COS-OGA |

### Monitoring/Enforcement methods

| | |
|---|---|
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | No method required |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | No method required |
| Soil (principle of method and LOQ) | Open |
| Water (principle of method and LOQ) | Open |
| Air (principle of method and LOQ) | Open |
| Body fluids and tissues (principle of method and LOQ) | Open |

### Classification and proposed labelling (Annex IIA, point 10)

| | |
|---|---|
| with regard to physical/chemical data | Not classified |

## Impact on Human and Animal Health

### Preliminary remark regarding the waiving of toxicological studies, reference values and exposure risk assessment:

COS (chito-oligosaccharides)-OGA (oligo-galacturonic acid) is an oligosaccharide complex.

- Chito-oligosaccharides, derived from chitosan (3rd polymer most present on earth) and COS, its oligomer, when released in the environment, are depolymerised into glucosamine. Purified chitin, chitosan, chito-oligomers and glucosamine, beside their natural occurrence, are used in the biomedical field such as targeted drug delivery. Chitin and chitosan (COS) are a family of linear polysaccharides consisting of varying amounts of β(1-4)linked residues of N-acetyl-2 amino-2-deoxy-D-glucose and 2 amino-2-deoxy-D-glucose residues. Chitin is the second most abundant natural polymer in nature after cellulose and is found in the structure of a wide number of invertebrates and the cell walls of fungi, among others.
- In the same way, pectin (2nd polymer most present on earth) and OGA, its oligomer, when released in the environment, are depolymerised into galacturonic acid. Pectin is one of the most important sources of dietary fibre. Pectin (OGA) is a family of complex polysaccharides (long linear chains of α-1,4-glycoside-linked D galacturonic acid) present in all plant primary cell walls. Pectin oligosaccharides represent a daily consumption in a Western diet between 4 and 5 g/day.

  Pectin is used as a food additive. OGA is obtained from pectin and COS is obtained from hydrolysis of chitosan.
- Various reliable studies were supplied concerning the toxicological profile of chitosan, COS and glucosamine as well as OGA. None of these studies reported significant adverse effects.
- Conclusion: both the studies conducted by the applicant and those published in the open scientific literature are considered sufficient for the risk-assessment of COS-OGA. Taking into account (i) the absence of adverse effects and (ii) the high background level of abovementioned substances, there is no need for the establishment of reference doses.

### Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

| | |
|---|---|
| Rate and extent of oral absorption ‡ | OGA: low but rapid<br>COS: important (> 85 %) and rapid |
| Distribution ‡ | Widely and evenly distributed |
| Potential for accumulation ‡ | No potential for accumulation |
| Rate and extent of excretion ‡ | No accumulation |
| Metabolism in animals ‡ | OGA: requires bacterial fermentation in large intestine giving a spectrum of short chain fatty acids and gases.<br>COS: is degraded into glucosamine further metabolised into $CO_2$, water and urea. |
| Toxicologically relevant compounds ‡ (animals and plants) | Not toxicologically relevant: OGA is obtained from pectin and COS is obtained from hydrolysis of chitosan. |
| Toxicologically relevant compounds ‡ (environment) | Not toxicologically relevant: OGA is obtained from pectin and COS is obtained from hydrolysis of chitosan. |

### Acute toxicity (Annex IIA, point 5.2)

| | | |
|---|---|---|
| Rat $LD_{50}$ oral ‡ | Female: > 5000 mg/kg bw | - |
| Rat $LD_{50}$ dermal ‡ | No study, not necessary | - |
| Rat $LC_{50}$ inhalation ‡ | No study, not necessary | - |
| Skin irritation ‡ | Non-irritant (*in vivo* and *in vitro* Episkin test) | - |

| | | |
|---|---|---|
| Eye irritation ‡ | Non-irritant | - |
| Skin sensitisation ‡ | Not sensitising (LLNA) | - |

**Short term toxicity (Annex IIA, point 5.3)**

| | | |
|---|---|---|
| Target / critical effect ‡ | No target organ, no adverse effect seen in published studies performed with either COS or OGA in separate studies | |
| Relevant oral NOAEL ‡ | Not required | |
| Relevant dermal NOAEL ‡ | Not required | |
| Relevant inhalation NOAEL ‡ | Not required | |

**Genotoxicity ‡ (Annex IIA, point 5.4)**

| | |
|---|---|
| Ames test is negative.<br>Published studies are negative, no further data required | |

**Long term toxicity and carcinogenicity (Annex IIA, point 5.5)**

| | | |
|---|---|---|
| Target/critical effect ‡ | No studies, not required | |
| Relevant NOAEL ‡ | - | |
| Carcinogenicity ‡ | Not carcinogenic | |

**Reproductive toxicity (Annex IIA, point 5.6)**

**Reproduction toxicity**

| | | |
|---|---|---|
| Reproduction target / critical effect ‡ | No studies, no adverse effect seen in a published study performed with OGA, not required | |
| Relevant parental NOAEL ‡ | - | |
| Relevant reproductive NOAEL ‡ | - | |
| Relevant offspring NOAEL ‡ | - | |

**Developmental toxicity**

| | | |
|---|---|---|
| Developmental target / critical effect ‡ | No studies, not required | |
| Relevant maternal NOAEL ‡ | - | |
| Relevant developmental NOAEL ‡ | - | |

**Neurotoxicity (Annex IIA, point 5.7)**

| | | |
|---|---|---|
| Acute neurotoxicity ‡ | No data, not necessary | |

| | | |
|---|---|---|
| Repeated neurotoxicity ‡ | No data, not necessary | |
| Delayed neurotoxicity ‡ | No data, not necessary | |

**Other toxicological studies (Annex IIA, point 5.8)**

| | |
|---|---|
| Mechanism studies ‡ | No data, not necessary |
| Studies performed on metabolites or impurities ‡ | No adverse effect seen in a published study performed with glucosamine. No relevant impurities |

**Medical data (Annex IIA, point 5.9)**

| |
|---|
| No incident occurred during production and handling of the pilot batches |

**Summary (Annex IIA, point 5.10)**

| | Value | Study | Uncertainty factor |
|---|---|---|---|
| ADI ‡ | Not relevant | - | - |
| AOEL ‡ | Not relevant | - | - |
| ARfD ‡ | Not relevant | - | - |

**Dermal absorption (Annex IIIA, point 7.3)‡**

| | |
|---|---|
| Formulation (e.g. name 50 % EC) | Due to the high molecular weight of a.s., its hydrophilic properties, and absence of solvents in formulation, significant dermal absorption is not expected. |

**Exposure scenarios (Annex IIIA, point 7.2)**

**Fyto11**

| | |
|---|---|
| Operator | Not required |
| Workers | Not required |
| Bystanders and residents | Not required |

**Classification and labelling with regard to toxicological data (Annex IIA, point 10)**

| | |
|---|---|
| Substance classified | COS-OGA |
| Harmonised classification | Currently not listed in Annex VI of Regulation (EC) No 1272/2008[7] (as amended) |
| RMS/peer review proposal[8] | none |

[7] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, 1-1355.

[8] It should be noted that proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals. Classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008.

### Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

| | |
|---|---|
| Plant groups covered | No data available; No data required |
| Rotational crops | No data available; No data required |
| Metabolism in rotational crops similar to metabolism in primary crops? | No data available; No data required |
| Processed commodities | No data available; No data required |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | No data available; No data required |
| Plant residue definition for monitoring | Not applicable |
| Plant residue definition for risk assessment | Not applicable |
| Conversion factor (monitoring to risk assessment) | Not applicable |

### Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

| | |
|---|---|
| Animals covered | No data available; No data required |
| Time needed to reach a plateau concentration in milk and eggs | No data available; No data required |
| Animal residue definition for monitoring | Not applicable |
| Animal residue definition for risk assessment | Not applicable |
| Conversion factor (monitoring to risk assessment) | Not applicable |
| Metabolism in rat and ruminant similar (yes/no) | No data available; No data required |
| Fat soluble residue: (yes/no) | Not applicable |

### Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

| |
|---|
| No data available; No data required |

### Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

| |
|---|
| No data available; No data required |

### Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

| | Ruminant: | Poultry: | Pig: |
|---|---|---|---|
| | Conditions of requirement of feeding studies | | |
| Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level) | n/a | n/a | n/a |
| Potential for accumulation (yes/no): | n/a | n/a | n/a |
| Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no) | n/a | n/a | n/a |
| | Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant)<br>Residue levels in matrices : Mean (max) mg/kg | | |
| Muscle | n/a | n/a | n/a |
| Liver | n/a | n/a | n/a |
| Kidney | n/a | n/a | n/a |
| Fat | n/a | n/a | n/a |
| Milk | n/a | | |
| Eggs | | n/a | |

n/a: not applicable

**Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)**

| Crop | Northern or Mediterranean Region, field or glasshouse, and any other useful information | Trials results relevant to the representative uses<br><br>(a) | Recommendation/comments | MRL estimated from trials according to the representative use | HR<br><br>(c) | STMR<br><br>(b) |
|---|---|---|---|---|---|---|
| No data available; No data required | | | | | | |

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

## Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

| | |
|---|---|
| ADI | Not applicable |
| TMDI (% ADI) according to WHO European diet | Not applicable |
| TMDI (% ADI) according to national (to be specified) diets | Not applicable |
| IEDI (WHO European Diet) (% ADI) | Not applicable |
| NEDI (specify diet) (% ADI) | Not applicable |
| Factors included in IEDI and NEDI | Not applicable |
| ARfD | Not applicable |
| IESTI (% ARfD) | Not applicable |
| NESTI (% ARfD) according to national (to be specified) large portion consumption data | Not applicable |
| Factors included in IESTI and NESTI | Not applicable |

## Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

| Crop/ process/ processed product | Number of studies | Processing factors | | Amount transferred (%) (Optional) |
|---|---|---|---|---|
| | | Transfer factor | Yield factor | |
| No data available; No data required | | | | |

## Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

It is proposed to consider the active substance COS-OGA for inclusion in Annex IV of Reg. (EC) No 396/2005.

**Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)**

| | |
|---|---|
| Mineralization after 100 days ‡ | The degradation of COS-OGA in soil by microorganisms is expected to lead to monomers (glucosamine and galacturonic acid) that will be further mineralized into $CO_2$, $H_2$ and $CH_4$ |
| Non-extractable residues after 100 days ‡ | No data available. |
| Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum) | No data available |

**Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)**

Anaerobic degradation ‡

| | |
|---|---|
| Mineralization after 100 days | No data available |
| Non-extractable residues after 100 days | No data available |
| Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum) | No data available. Dissociated polymers COS (chitosan) and OGA (partially hydrolised pectin) are expected to occur outside of the range of pH 3.6 to 6.5. |

Soil photolysis ‡

| | |
|---|---|
| Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum) | No data available |

### Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

No data available. Use evaluated restricted to permanent greenhouses

Field studies ‡

No data available.

| | |
|---|---|
| pH dependence ‡ (yes / no) (if yes type of dependence) | Yes, complex COS-OGA is expected to be dissociated out of the range pH 3.6 to 6.5. |
| Soil accumulation and plateau concentration ‡ | No data available. Use evaluated restricted to permanent greenhouses |

### Soil adsorption/desorption (Annex IIA, point 7.1.2)

No data available. Use evaluated restricted to permanent greenhouses

### Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

| | |
|---|---|
| Column leaching ‡ | Not available, not required |
| Aged residues leaching ‡ | Not available, not required |
| Lysimeter/ field leaching studies ‡ | Not available, not required |

### PEC (soil) (Annex IIIA, point 9.1.3)

| | |
|---|---|
| Parent<br>Method of calculation | No data available. Use evaluated restricted to permanent greenhouses |
| Application data | - |

| **PEC$_{(s)}$** (mg/kg) | Single application<br>Actual | Single application<br>Time weighted average | Multiple application<br>Actual | Multiple application<br>Time weighted average |
|---|---|---|---|---|
| | Not calculated, not required for the representative use in greenhouses. | Not calculated, not required for the representative use in greenhouses. | Not calculated, not required for the representative use in greenhouses. | Not calculated, not required for the representative use in greenhouses. |

## Route and rate of degradation in water (Annex IIA, point 7.2.1)

| | |
|---|---|
| Hydrolytic degradation of the active substance and metabolites > 10 % ‡ | No data available. Complex COS-OGA is expected to be dissociated out of the range pH 3.6 to 6.5. The separated components COS and OGA are expected to be stable to hydrolysis under normal environmental conditions. |
| Photolytic degradation of active substance and metabolites above 10 % ‡ | No data available. Expected to be stable to aqueous photolysis under normal environmental conditions |
| Quantum yield of direct phototransformation in water at Σ > 290 nm | No data available. |
| Readily biodegradable ‡ (yes/no) | No reliable study available. Data gap identified.<br>In the absence of further data COS-OGA should be considered not readily biodegradable. |

**Degradation in water / sediment**

No data available.

## PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

| | |
|---|---|
| Parent<br>Parameters used in FOCUSsw step 1 and 2 | 0.21 µg/L based on the greenhouse use with a 0.2 % emission |
| Parameters used in FOCUSsw step 3 (if performed) | - |
| Metabolite X<br>Parameters used in FOCUSsw step 1 and 2 | Not calculated for the separated componets COS and OGA |

## PEC (ground water) (Annex IIIA, point 9.2.1)

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter ) | No data available. Use evaluated restricted to permanent greenhouses |

**PEC**$_{(gw)}$ From lysimeter / field studies

No data available. Not required.

## Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

| | |
|---|---|
| Direct photolysis in air ‡ | No data available |
| Quantum yield of direct phototransformation | No data available |
| Photochemical oxidative degradation in air ‡ | No data available |
| Volatilisation ‡ | -No data available |
| | No data available |
| Metabolites | No data available |

### PEC (air)

| | |
|---|---|
| Method of calculation | No data available |

### $PEC_{(a)}$

| | |
|---|---|
| Maximum concentration | No data available |

### Residues requiring further assessment

| | |
|---|---|
| Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology). | Soil: COS-OGA, COS (chitosan), OGA (partially hydrolised pectin)<br>Surface Water: -COS-OGA, COS (chitosan), OGA (partially hydrolised pectin)<br>Sediment: COS-OGA, COS (chitosan), OGA (partially hydrolised pectin)<br>Ground water: COS-OGA, COS (chitosan), OGA (partially hydrolised pectin)<br>Air: COS-OGA |

### Monitoring data, if available (Annex IIA, point 7.4)

| | |
|---|---|
| Soil (indicate location and type of study) | Not available |
| Surface water (indicate location and type of study) | Not available |
| Ground water (indicate location and type of study) | Not available |
| Air (indicate location and type of study) | Not available |

### Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

| |
|---|
| No readily biodegradable (in absence of reliable biodegradation study). |

### Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

| Species | Test substance | Time scale | End point (mg/kg bw/day) | End point (mg/kg feed) |
|---|---|---|---|---|
| Birds ‡ | | | | |
| Two subchronic studies were conducted to assess the effect of pectin and chitosan in broiler chickens. Neither pectin nor chitosan presented any relevant adverse effect, even after ingestion of 30 g/kg of feed during at least 10 days. | | | | |
| Mammals ‡ | | | | |
| rat | COS-OGA | Acute | > 5000 | - |
| rat | FYTO11 | Acute | > 2000 | - |
| Additional higher tier studies ‡ | | | | |
| Not required. | | | | |

### Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)*

Crop and application rate: cucumber, 5 x 0.025 kg a.s./ha LWA

| Indicator species/Category[2] | Time scale | ETE | TER[1] | Annex VI Trigger[3] |
|---|---|---|---|---|
| Tier 1– uptake via diet (Mammals) | | | | |
| Small herbivorous mammal | Acute | 6.48 | > 772 | 10 |

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

Crop and application rate: cucumber, 5 x 0.063 kg a.s./ha soil

| Indicator species/Category[2] | Time scale | ETE | TER[1] | Annex VI Trigger[3] |
|---|---|---|---|---|
| Tier 1– uptake via diet (Mammals) | | | | |
| Small herbivorous mammal | Acute | 16.33 | > 306 | 10 |

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

* A quantitative risk assessment was not performed for birds as based on the representative uses on permanent glasshouses the exposure to COS-OGA was considered negligible. Similarly due to the intrinsic characteristics of COS-OGA no long term risk assessment was deemed necessary for mammals.

### Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

| Group | Test substance | Time-scale (Test type) | End point | Toxicity[1] (mg/L) |
|---|---|---|---|---|
| Laboratory tests ‡ | | | | |
| Fish | | | | |
| *Danio rerio* | COS-OGA | 7 d (semi-static) | Mortality,<br>$EC_{50}$<br>NOEC | <br>228 mg/L*<br>20 mg/L* |

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.
*****The maintenance of the test item concentration in water during the test was not confirmed, therefore the study cannot be considered valid

The published literature data on the effects of chitin and chitosan when administered to the diet of several fish species demonstrate a beneficial effect by enhancing the immune response and resistance against diseases.

## Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

During the Peer Review, the exposure was calculated with $PEC_{SW}$ = 0.21 µg a.s./L (refer to Volume 3 B.8 on fate and behavior). The corresponding TER calculations for fish are presented in the Table below.

Acute and chronic risk to fish based on Early Life Stage toxicity test from exposure to the formulation FYTO11 following the use in cucumber

| Test substance | Test species | Test system | Endpoint (mg a.s./L) | $PEC_{SW}$ (µg a.s./L) | TER | Annex VI trigger value |
|---|---|---|---|---|---|---|
| COS-OGA | *Danio rerio* | ELS, 7 days | $EC_{50}$ = 228 | 0.21 | 1085714 | 100 |
| | | | NOEC = 20 | 0.21 | 95238 | 10 |

In conclusion, taking into account that the formulation FYTO11 is recommended for use in greenhouses, the likely degradation of the active substance COS-OGA into negligible quantities of COS and OGA compared to the large amounts of COS and OGA naturally present, the exposure to aquatic organisms is considered negligible. Also, no adverse effects of COS and OGA were reported in literature. Therefore low risk to aquatic organisms for the proposed use of FYTO11 is concluded.

| **Bioconcentration** |
|---|
| The active substance COS-OGA is easily degraded in water by the action of many enzymes secreted by a large spectrum of microorganisms (refer to Volume 3 B.8 on fate and behavior). The respective quantities of COS and OGA resulting from the use of COS-OGA is negligible compared to the large amounts of COS and OGA as well as their metabolites (glucosamine and galacturonic acid) naturally present in water.<br>Moreover, these two metabolites are likely mineralised into $CO_2$, $H_2$ and $CH_4$ (refer to Volume 3 B.8 on fate and behavior).<br>Finally, the active substance COS-OGA is extremely hydrophilic (refer to Volume 3 B.2 on physical chemical properties) and therefore bioaccumulation in fish is not expected. |

[1] only required if log $P_{O/W}$ >3.
* based on total $^{14}C$ or on specific compounds

## Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

| Test substance | Acute oral toxicity ($LD_{50}$ µg/bee) | Acute contact toxicity ($LD_{50}$ µg/bee) |
|---|---|---|
| FYTO11 | > 10.0 µg COS-OGA/bee | > 12.5 µg COS-OGA/bee |

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

## Hazard quotients for honey bees (Annex IIIA, point 10.4)

Crop and application rate: cucumber, 5 x 0.025 kg a.s./ha LWA

| Test substance | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|
| FYTO11 | contact | < 2.0 | 50 |
| FYTO11 | oral | < 2.5 | 50 |

Crop and application rate: cucumber, 5 x 0.063 kg a.s./ha soil

| Test substance | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|

| Test substance | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|
| FYTO11 | contact | < 5.0 | 50 |
| FYTO11 | oral | < 6.3 | 50 |

**Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)**

Laboratory tests with standard sensitive species

| Species | Test Substance | End point | Effect ($LR_{50}$ L/ha[1]) |
|---|---|---|---|
| *Typhlodromus pyri* ‡ | FYTO11 | Mortality | 4.97 L/ha |

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Cucumber under glasshouse 5x25 g a.s./ha Leaf Wall Area (corresponding to 2 L formulation FYTO11/ha*)

| Test substance | Species | Effect ($LR_{50}$ L/ha) | HQ in-field | HQ off-field[1] | Trigger |
|---|---|---|---|---|---|
| FYTO11 | *Typhlodromus pyri* | 4.97 L/ha | < 1.21 | < 0.022 (at 1 m, < 50 cm)<br>< 0.080 (at 3 m, > 50 cm) | 2 |

[1] indicate distance assumed to calculate the drift rate

Further laboratory and extended laboratory studies ‡

| Species | Life stage | Test substance, substrate and duration | Dose (L/ha)[1,2] | End point | % effect[3] | Trigger value |
|---|---|---|---|---|---|---|
| *Aphidius rhopalosiphi*[4] | adults | FYTO11, barley seedlings | 0.5 %,<br>1.0 %<br>FYTO11 | $M_{cor}$<br>$M_{cor}$ | -1.1 %<br>-7.6 % | 50 %<br>50 % |
| *Episyrphus balteatus*[4] | larvae | FYTO11, sweet-pepper plants | 0.5 %,<br>1.0 %<br>FYTO11 | $M_{cor}$<br>$M_{cor}$ | 5.4 %<br>-2.7% | 50 %<br>50 % |

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation
[3] indicate if positive percentages relate to adverse effects or not
[4] it is not clear whether the tested concentration cover the representative uses as reported in the GAP. The study was not performed under the GLP.

| Field or semi-field tests |
|---|
| Not required. |

***Consideration about the expression of the dose and the risk assessment for non-target terrestrial arthropods**

As shown in the GAP table (Volume 1 point 1.5), the dose of 25 g a.s./ha (or 2 L formulation/ha) is expressed as a dose per ha Leaf Wall Area. This dose corresponds to a dose of 63 g a.s./ha soil (assuming a distance between rows of 1.6 m and a treated height of plants of 2 m).

The risk assessment for non-target terrestrial arthropods carried out above is considered as relevant for the representative uses expressed in Leaf Wall Area (*i.e.* 25 g a.s./ha LWA) as the arthropods living on the leaves of the treated crop are really exposed to the dose of 25 g a.s./ha (*i.e.* 2 L formulation/ha).

**Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)**

Since the active substance COS-OGA is easily degraded in the environment by the action of many enzymes secreted by a large spectrum of microorganisms (refer to Volume 3 B.8 on fate and behavior) and the respective quantities of COS and OGA resulting from the use of COS-OGA is negligible compared to the large amounts of COS and OGA naturally present in the environment, it is not considered necessary to conduct further testing.

### Toxicity/exposure ratios for soil organisms

Taking into account that the formulation FYTO11 is recommended for use in greenhouses, the likely degradation of the active substance COS-OGA into negligible quantities of COS and OGA compared to the large amounts of COS and OGA naturally present, the exposure to earthworms, other soil macro-organisms and other soil micro-organisms, is considered negligible. Also, no adverse effects of COS and OGA were reported in literature. Therefore low risk to earthworms, other soil macro-organisms and other soil micro-organisms for the proposed use of FYTO11 is concluded.

### Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

In general, there is no effect expected on the crop and on terrestrial non-target plants other than to trigger the plant defences to face the pathogen.

### Effects on biological methods for sewage treatment (Annex IIA 8.7)

Since the active substance COS-OGA is easily degraded in the environment by the action of many enzymes secreted by a large spectrum of microorganisms (refer to Volume 3 B.8 on fate and behavior) and the respective quantities of COS and OGA resulting from the use of COS-OGA is negligible compared to the large amounts of COS and OGA naturally present in the environment, it is not considered necessary to conduct further testing.

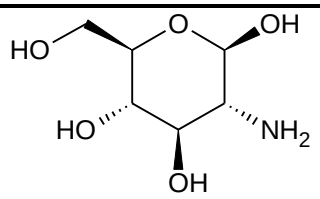
**Ecotoxicologically relevant compounds** (consider parent and all relevant metabolites requiring further assessment from the fate section)

| Compartment | |
|---|---|
| soil | - |
| water | - |
| sediment | - |
| groundwater | - |

**Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)**

| | RMS/peer review proposal |
|---|---|
| Active substance | - |

## APPENDIX B – USED COMPOUND CODE(S)

| Code/Trivial name* | Chemical name/SMILES notation** | Structural formula** |
|---|---|---|
| **glucosamine** | 2-amino-2-deoxy-□-D-glucopyranose<br><br>O[C@H]1[C@H](O)[C@@H](CO)O[C@@H](O)[C@@H]1N |  |



* The metabolite name in bold is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

## ABBREVIATIONS

| | |
|---|---|
| ε | decadic molar extinction coefficient |
| °C | degree Celsius (centigrade) |
| µg | microgram |
| µm | micrometer (micron) |
| a.s. | active substance |
| ADI | acceptable daily intake |
| AOEL | acceptable operator exposure level |
| ARfD | acute reference dose |
| AV | avoidance factor |
| bw | body weight |
| CAS | Chemical Abstracts Service |
| CIPAC | Collaborative International Pesticides Analytical Council Limited |
| cm | centimetre |
| d | day |
| DAR | draft assessment report |
| $EC_{50}$ | effective concentration |
| EEC | European Economic Community |
| EINECS | European Inventory of Existing Commercial Chemical Substances |
| ELINCS | European List of New Chemical Substances |
| ELS | early-life-stage |
| EMDI | estimated maximum daily intake |
| EU | European Union |
| FAO | Food and Agriculture Organization of the United Nations |
| FOCUS | Forum for the Co-ordination of Pesticide Fate Models and their Use |
| g | gram |
| GAP | good agricultural practice |
| GCPF | Global Crop Protection Federation (formerly known as GIFAP) |
| GHS | Globally Harmonized System of Classification and Labeling of Chemicals |
| h | hour(s) |
| ha | hectare |
| hL | hectolitre |
| HQ | hazard quotient |
| HR | highest residue |
| IEDI | international estimated daily intake |
| IESTI | international estimated short-term intake |
| ISO | International Organization for Standardization |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram |
| L | litre |
| $LC_{50}$ | lethal concentration, median |
| $LD_{50}$ | lethal dose, median; dosis letalis media |
| LLNA | local lymph node assay |
| LOQ | limit of quantification (determination) |
| $LR_{50}$ | lethal rate |
| LWA | leaf wall area |
| m | metre |
| mg | milligram |
| mm | millimetre (also used for mean measured concentrations) |
| mN | milli-newton |
| MRL | maximum residue limit or level |
| NEDI | national estimated daily intake |
| NESTI | national estimated short-term intake |
| NOAEL | no observed adverse effect level |

| | |
|---|---|
| NOEC | no observed effect concentration |
| OECD | Organisation for Economic Co-operation and Development |
| Pa | pascal |
| PD | proportion of different food types |
| PEC | predicted environmental concentration |
| $PEC_{air}$ | predicted environmental concentration in air |
| $PEC_{gw}$ | predicted environmental concentration in ground water |
| $PEC_{sed}$ | predicted environmental concentration in sediment |
| $PEC_{soil}$ | predicted environmental concentration in soil |
| $PEC_{sw}$ | predicted environmental concentration in surface water |
| pH | pH-value |
| PHI | pre-harvest interval |
| $P_{ow}$ | partition coefficient between *n*-octanol and water |
| PT | proportion of diet obtained in the treated area |
| RMS | rapporteur Member State |
| SANCO | Directorate-General for Health and Consumers |
| SMILES | simplified molecular-input line-entry system |
| STMR | supervised trials median residue |
| TER | toxicity exposure ratio |
| TMDI | theoretical maximum daily intake |
| UV | ultraviolet |
| WHO | World Health Organization |