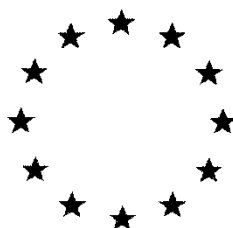


European Commission



**Draft Renewal Assessment Report prepared according to the Commission
Regulation (EU) N° 1107/2009**

Microbial Pest Control Agent (MPCA)
Bacillus thuringiensis
subsp. *kurstaki* SA-12

Volume 3 – B.6 (PPP) – CoStar WG
Effects on human health

Rapporteur Member State: Denmark
Co- Rapporteur Member State: The Netherlands

Version history

When	What
2008	DAR
2011	Addendum to the DAR
2019	Initial RAR

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B.6 Effects on human health

INTRODUCTION

Bacillus thuringiensis subsp. *kurstaki* SA-12 (in the following abbreviated as Btk SA-12) was one of the existing active substances covered by the Regulation (EC) No 2229/2004 on the implementation of the fourth stage of the program of work referred to in Article 8(2) of Council Directive 91/414/EEC. In Annex I to Regulation (EC) No 2229/2004 the Commission designated Denmark as rapporteur Member State to carry out the assessment of Btk SA-12 on the basis of a joint dossier submitted for the Btk strains SA-11, SA-12 and EG 2348. The notifier for Btk SA-11 and SA-12 was Mitsui AgriScience International SA/NV while EG 2348 was notified by Mitsui AgriScience International SA/NV and Intrachem Bio Italia S.p.A. (now CBC (Europe) S.r.l.). In accordance with the provisions of Article 22(1) of Regulation (EC) No 2229/2004, Denmark submitted in January and February 2008 to the EFSA the draft assessment report, including, as required, a recommendation concerning the possible inclusion of Btk SA-12 in Annex I to the Directive. The Commission examined the draft assessment report, the recommendations by the rapporteur Member State and the comments received from other Member States in consultation with experts from a certain number of Member States. The Commission referred on 11 July 2008 a draft review report to the Standing Committee on the Food Chain and Animal Health, for final examination. The draft review report was finalized in the meeting of the Standing Committee on 11 July 2008. Subsequently Regulation (EC) No 1107/2009 repealed and replaced Directive 91/414/EEC and the active substance Btk SA-12, was deemed to be approved under that Regulation and included in the Annex to Regulation (EC) No 540/2011. EFSA delivered its conclusions on *Bacillus thuringiensis* ssp. *kurstaki* (strains ABTS-351, PB-54, SA-11, SA-12, EG2348) on the 16 December 2011 (published 23 February 2012). Based on this new information available, no need to change the conditions of approval of Btk SA-12 was identified. The Commission filed on 13 December 2013 an updated review report for Btk strains SA-11, SA-12 and EG 2348 to the Standing Committee on the Food Chain and Animal Health for examination.

The approval of Btk SA-12 under the Regulation (EC) No 1107/2009 expires 30 April 2019. In accordance with the same Regulation the original notifier Mitsui AgriScience International SA/NV has filed to the Commission an application for the renewal of the approval of the active substance Btk SA-12 on 30 April 2016. In accordance with Regulation (EU) 2016/183 the notifier submitted to the designated RMS Denmark, the co-RMS The Netherlands as well as to EFSA and Commission a dossier for renewal of Btk SA-12 considering the deadline stated in SANTE-2016-10616–rev. 3.

Btk SA-12 is a wild type strain originating from infested insects. Btk acts highly specific against insect species of the order Lepidoptera and is not expected to have any harmful effects on beneficials and other non-target species of other insect orders. The insecticidal activity of Btk is mainly attributed to spore bound insecticidal pro-proteins (Cry toxins) which are ingested by the target pests and activated under alkaline conditions in the midgut of the larvae. The first assessment of the strain proved that it does not have any harmful effects on human or animal health or on groundwater or any unacceptable influence on the environment. The overall conclusion from EFSA (2012) confirms that no critical areas of concern are identified within the framework of the use which was supported.

The representative formulation for renewal of the approval of Btk SA-12 under Regulation (EC) 1107/2009 is CoStar WG. CoStar WG is a WG formulation having a biopotency of 90000 IU/mg. The content of the active ingredient is 85% corresponding to a maximum of 5.7×10^{13} CFU/kg product. CoStar WG was not the representative formulation for original approval of the strain. Therefore, no data have been submitted for this formulation before. However, CoStar WG, except for the active ingredient, is identical to the representative formulation for original approval, Delfin WG, containing Btk SA-11. Also the two Btk strains are very similar with regard to their biological properties and physiological requirements. It is therefore justified to use data for Delfin WG also for the evaluation of CoStar WG. In addition, the manufacturing process of SA-12 has not been changed since original approval all data previously submitted and referring to Btk SA-12 are considered fully applicable for the current evaluation.

In the following for ease of information, full study summaries/sections taken from the DAR (2008) or its Final Addendum (2011) are included if they are considered relevant for renewal of Btk SA-12. In order to facilitate discrimination between new data and data already evaluated during the first approval process, the headline “New information” begins the section with data, which have previously not been submitted or evaluated. Data and their evaluations from the original DAR and addenda to the DAR are highlighted by grey background. There might be some exceptions but in this case justifications/explanations are provided.

Representative uses chosen for renewal of Btk SA-12 cover control of *Cydia pomonella* in pome fruits and *Spodoptera* spp. in ornamentals as field uses, as well as *Tuta absoluta* in tomato in the greenhouse. Both, use by

professionals and non-professionals is intended. Application rates range between 1 – 2 kg with 6 subsequent applications at an interval of 7 days.

It is considered that the Critical GAP of CoStar WG chosen for the renewal of the active substance Btk SA-12 covers worst case exposure scenarios for human, non-target organisms and the environment.

Critical GAP of CoStar WG for renewal of Btk SA-12

Crop	F G or I	Pest	Application			Application rate		
			Method / Kind	Growth stage of crop	Max. number (min. interval between applications) a) per use b) per crop/season	Kg product / ha a) max. rate per appl. b) max. total rate per crop/season	g as/ha IU/ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min / max
Pome fruits	F	<i>Cydia pomonella</i>	Foliar spray	BBCH 67-89	a) 6 (7) b) 6 (7)	a) 1.5 b) 9.0	a) $1275 / 1.35 \times 10^{11}$ b) $7650 / 8.1 \times 10^{11}$	1000-1500
Tomato	G	<i>Tuta absoluta</i>	Foliar spray	BBCH 12-89	a) 6 (7) b) 6 (7)	a) 1.0 b) 6.0	a) $850 / 9.0 \times 10^{10}$ b) $5100 / 5.4 \times 10^{11}$	200-1000
Ornamentals	F	<i>Spodoptera</i> spp.	Foliar spray	BBCH 12-89	a) 6 (7) b) 6 (7)	a) 2.0 b) 12.0	a) $1700 / 1.8 \times 10^{11}$ b) $10200 / 1.1 \times 10^{12}$	500-1000

Biopotency of CoStar WG: 90000 IU/mg

Max. CFU content in CoStar WG: 5.7×10^{13} CFU/kg

B.6.1 Basic acute toxicity studies

As CoStar WG was not the representative formulation for original approval of Btk SA-12, no data on the formulation have been submitted before.

New data 2016

No study assessing the effect of CoStar WG on human health is submitted here. It is referred to the information submitted for *Bacillus thuringiensis* subsp. *kurstaki* SA-12 in Vol.3 MA, Section B.6, Point B.6.1.

The ingredients of the preparation CoStar WG, formulated as water dispersible granule, are inert and no hazards to the human health are expected (please refer to Volume 4). Therefore, studies and information on the microbial pest control agent, *Bacillus thuringiensis* subsp. *kurstaki* SA-12, are considered applicable and relevant with regard to the evaluation of effects on mammals of the formulated products.

B.6.1.1 Acute oral toxicity

As CoStar WG was not the representative formulation for original approval of Btk SA-12 no data on the formulation have been submitted before.

New data 2016

It is referred to the information submitted for *Bacillus thuringiensis* subsp. *kurstaki* SA-12 in Vol. 3 MA, Section B.6, Point B.6.1.2.2. During first approval, data for the formulations Delfin WG and Javelin WG have been submitted. Delfin WG and Javelin WG contain Btk SA-11 which is closely related and very similar to Btk SA-12. In addition, Delfin WG/Javelin WG and CoStar WG are identical with regard to the product composition. The studies on Delfin WG/Javelin WG are therefore considered fully applicable to assess possible effects of CoStar WG on acute oral toxicity.

Moreover, the ingredients of the preparation CoStar WG, formulated as water dispersible granule, are inert and no hazards to the human health are expected (please refer to Volume 4). Therefore, studies and information on the microbial pest control agent, *Bacillus thuringiensis* subsp. *kurstaki* SA-12, are considered applicable and relevant with regard to the evaluation of effects on mammals of the formulated products.

Thus, CoStar WG does not warrant classification as being toxic or harmful on the basis of its acute oral toxicity according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. No hazard statement or signal word is required.

RMS conclusion	<p>The ingredients of the preparation CoStar WG are inert and no hazards to the human health are expected. Therefore, studies and information on the microbial pest control agent, <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12, are considered applicable and relevant with regard to the evaluation of acute oral toxicity on mammals of the formulated products.</p> <p>Based on a new study conducted according to OPPTS 885.3050 Microbial pesticide test guidelines (please refer to Vol. 3 MA, Section B.6, point B.6.1.2.2) it is concluded, that Btk SA-12 does not warrant classification as being toxic or harmful based on its acute oral toxicity. Consequently, CoStar WG does not require classification with regard to acute oral toxicity according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. No hazard statement or signal word is required.</p>
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B.6.1.2 Acute inhalation toxicity

As CoStar WG was not the representative formulation for original approval of Btk SA-12 no data on the formulation have been submitted before.

New data 2016

It is referred to the information submitted for *Bacillus thuringiensis* subsp. *kurstaki* SA-12 in Volume 3, MA B.6.1.2.2.

The ingredients of the preparation CoStar WG, formulated as water dispersible granule, are inert and no hazards to the human health are expected (please refer to Volume 4). Therefore, studies and information on the microbial pest control agent, *Bacillus thuringiensis* subsp. *kurstaki* SA-12, are considered applicable and relevant with regard to the evaluation of effects on mammals of the formulated products.

Thus, CoStar WG does not warrant classification as being toxic or harmful on the basis of its acute respiratory toxicity according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. No hazard statement or signal word is required.

RMS conclusion	<p>The ingredients of the preparation CoStar WG are inert and no hazards to the human health are expected. Therefore, studies and information on the microbial pest control agent, <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12, are considered applicable and relevant with regard to the evaluation of acute oral toxicity on mammals of the formulated products.</p> <p>Based on a new study conducted according to OPPTS 885.3150 Microbial pesticide test guidelines (please refer to Vol. 3 MA, Section B.6, point B.6.1.2.2) it is concluded, that Btk SA-12 does not warrant classification as being toxic or harmful based on its acute pulmonary toxicity. Consequently, CoStar WG does not require classification with regard to acute pulmonary toxicity according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. No hazard statement or signal word is required.</p>
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B.6.1.3 Acute percutaneous toxicity

As CoStar WG was not the representative formulation for original approval of Btk SA-12 no data on the formulation have been submitted before.

New data 2016

It is referred to the information submitted for the technical active ingredient Btk SA-12 in Doc M-MA, Section 5, Point MA 5.3. In a dermal toxicity study in rats submitted during first approval of the active substance the LD₅₀ was determined to be greater than 5050 mg/kg. Moreover, it is referred to the information submitted for the representative formulation Delfin WG in Doc M-IIIM, Section 3, Point IIIM 7.1.2. Delfin WG/Javelin WG contains Btk SA-11 which is closely related and very similar to Btk SA-12 as indicated in the review report for *Bacillus thuringiensis* subsp. *kurstaki*, strains SA-11, SA-12 and EG2348¹, as well as the EFSA Conclusion². In addition, Delfin WG/Javelin WG and CoStar WG are identical with regard to the product composition (please refer to Volume 4). The study on Delfin WG/Javelin WG is therefore considered fully applicable to assess possible effects of CoStar WG on acute percutaneous toxicity.

Micro-organisms do not penetrate intact human skin. Hence, no study on dermal absorption was performed for CoStar WG and no default values are set for the concentrate and spray dilution.

¹ European Commission, 2008. Review Report for the active substance *Bacillus thuringiensis* subsp. *kurstaki* (strains SA 11, SA 12, EG 2348), SANCO/1543/08 – rev. 4, 13.12.2013

² European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance *Bacillus thuringiensis* ssp. *kurstaki* (strains ABTS 351, PB 54, SA 11, SA 12, EG 2348). EFSA Journal 2012; 10(2):2540.

Thus, CoStar WG does not require classification with regard to dermal toxicity according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. No hazard statement or signal word is required.

RMS conclusion	<p>The ingredients of the preparation CoStar WG are inert and no hazards to the human health are expected. Therefore, studies and information on the microbial pest control agent, <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12, are considered applicable and relevant. Furthermore, microorganisms will not penetrate the intact skin and no data are required.</p> <p>Thus, CoStar WG does not require classification with regard to dermal toxicity according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. No hazard statement or signal word is required.</p>
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B.6.2 Additional acute toxicity studies

B.6.2.1 Skin irritation

As CoStar WG was not the representative formulation for original approval of Btk SA-12 no data on the formulation have been submitted before.

The active ingredient Btk SA-12 should not be classified as being irritating to skin based on an acute dermal irritation study evaluated in the DAR 2008.

Report:	KMP 6.1.2/01 [REDACTED] (1999C) COSTAR TECHNICAL CONCENTRATE. ACUTE DERMAL IRRITATION STUDY IN RABBITS
Test substance/concentration:	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> strain SA-12, Lot no. 2731269
Guideline/GLP:	OPPTS 870.2500/Yes
Deviations:	None
Acceptability:	Yes
Species/strain:	Rabbit/New Zealand White
Doses/no. of animals:	Single dose of 0.5 g for four hours/3 males
Administration way/vehicle:	0.5 g on clipped area/moistened with deionized water
Test system:	Test sites were observed for erythema, oedema formation and other dermal defects or irritation at 1, 24, 48 and 72 hrs after unwrap

Findings:

Very slight erythema was present at each observation through 24 hours. Oedema was not observed at any time throughout the study. No other signs of irritation were observed during the study.

Score erythema: 24/48/72 hrs = 1/0/0 = 0.3 (mean)

Score oedema: 24/48/72 hrs = 0/0/0 = 0 (mean)

Conclusion:

According to Directive 67/548/EEC should the strain SA-12 not be classified since the mean value of scores for either erythema or oedema formation, calculated over all the animals at times of 24, 48 and 72 hrs, was less than 2.

New data 2016

In absence of data on the formulated product, evaluation of the skin irritating potential according to Annex I of Regulation (EC) No. 1272/2008 is applied.

The active ingredient Btk SA-12 is not classified as being irritating to skin according to the study evaluated in the DAR 2008 (Please see above).

Also the co-formulant contained in CoStar WG is not classified as being irritating to skin. Hence, according to Regulation (EC) No. 1272/2008 the product CoStar WG does not warrant classification for skin irritation. No hazard statement or signal word is required.

RMS conclusion	<p>The dermal irritating potential of the active ingredient Btk SA-12 was investigated in a study on dermal toxicity. The study was conducted according to the OPPTS 870.2500 guideline. The study is considered applicable to assess skin irritation of <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12 and shows Btk SA-12 should not be classified as being irritating to skin.</p> <p>Article 40 of the Pesticides Regulation provides that testing on vertebrates shall be undertaken only as a last resort. The use of non-animal test methods and other risk assessment strategies should be promoted. Animal testing for the purposes of this Regulation should be minimised and tests on vertebrates should be undertaken as a last resort. Seen in this context the available data on the active substance from first approval of Btk SA-12 are considered acceptable to cover current requirements. Also, the co-formulant contained in CoStar WG is not classified as being irritating to skin. Therefore, no new studies are required.</p> <p>CoStar WG does not require classification with regard to skin irritation according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.</p>
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B.6.2.2 Eye irritation

As CoStar WG was not the representative formulation for original approval of Btk SA-12 no data on the formulation have been submitted before.

The active ingredient Btk SA-12 was shown to be slightly irritating based on an eye irritation study already evaluated in the DAR 2008. However, in conclusion SA-12 should not be classified for eye irritation. Therefore a re-evaluation of the previously submitted study with the technical substance SAN 420I containing Btk SA-12 is included below.

Reference:	KMP 6.2.2/01
Report:	██████████ (1992) Eye Irritation to the Rabbit of SAN 420I (SA-12) technical Unpublished Report No. 920159D/SNC 151/SE
Guideline(s):	EPA FIFRA 152A-14/Yes
GLP:	Yes
Acceptability:	Yes
Duplication: (if vertebrate study)	No
Deviations	None

Executive summary

In a primary eye irritation study according to EPA FIFRA 152A-14 guideline, six rabbits were exposed to Single dose of 100 mg SAN 420 I (SA-12) technical, corresponding to 5.77×10^8 CFU of the active ingredient *Bacillus*

thuringiensis subsp. *kurstaki* SA-12. Three additional rabbit were administered a single ocular dose of 100mg of the test substance with the eyes washed with distilled water 30 seconds after instillation for a duration of 30 seconds. These animals were observed for a maximum of seven days after instillation. The test item was instilled into the conjunctival sac of one eye of each animal and the lids were gently held together for about 1 second in order to prevent loss of the test item. The untreated contralateral eye served as control. Irritation was scored according to guideline.

Instillation of SAN 420I (SA-12) technical into the rabbit eye elicited transient corneal dulling and slight conjunctival irritation. Whereas, instillation of SAN 420I (SA-12) technical into the rabbit eye following by rinsing elicited transient slight conjunctival irritation only.

Material and Methods

Test Item

Designation	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> strain SA-12, Batch no. P74-F13GPCG5/3/given by laboratory: 5.77×10^9 CFU/g.
Characteristics	Brown powder
Batch no.	F74-F13 GpCG5/3

Study Design and Methods

Performing laboratory	
Exposure	Instillation of 100 mg test item into the lower everted lid of one eye of each animal
Vehicle	None
Post exposure observation:	7 days
Experimental treatment	Eyes of each animal were examined prior to instillation of the test item. Approximately 100 mg of the test item were placed into the lower everted lid of one eye of each animal. The lids were gently held together for one second in order to prevent loss of the test item. The untreated contralateral eye served as control.
Observations	The eyes of all animals were examined for signs of irritation after 1h and 1, 2, 3, 4 and 7 days post exposure. Eye irritation was scored and recorded.

Findings

No mortalities were observed. No clinical signs of toxicity were noted. Unwashed animals: A dulling of the cornea in 4/6 animals at the one-hour reading only. Diffuse crimson-red colouration of the conjunctivae in 4/6 animals. In the two remaining animals there were mild conjunctival readings. Slight discharge was found in all animals. All responses had resolved seven days after installation.

Washed animals: A diffuse crimson-red colouration of the conjunctivae in 1/3 animals at the one-hour reading. Transient mild reactions was observed in the two other animals, and slight discharge in all three animals. All responses had resolved seven days after installation. (Table 6.2.2-1).

Table 6.2.2-1 Irritant response data for each animal at each observation time up to removal of each animal from the test

Score at time point / Reversibility	Cornea [Max. score: 4]	Iris [Max. score: 2]	Conjunctivae redness [Max. score: 3]	Chemosis [Max. score: 4]
60 min	D/D/D/0/D/0	0/0/0/0/0/0	1/1/1/1/2/1	1/1/1/1/1/1
24 h	0/0/0/0/0/0	0/0/0/0/0/0	2/1/2/2/2/1	1/1/1/1/1/1
48 h	0/0/0/0/0/0	0/0/0/0/0/0	2/1/2/2/2/1	1/1/1/1/1/1
72 h	0/0/0/0/0/0	0/0/0/0/0/0	1/1/1/1/1/1	1/1/1/1/1/1
4 day	0/0/0/0/0/0	0/0/0/0/0/0	1/1/1/1/1/1	1/1/0/0/1/1
7 day	0/0/0/0/0/0	0/0/0/0/0/0	0/0/0/0/0/0	0/0/0/0/0/0
Average (24 h, 48 h, 72 h)	0/0/0/0/0/0	0/0/0/0/0/0	1.7/1/1.7/1.7/1.7/1	1/1/1/1/1/1/1
Area affected	-	-	-	-
Maximum average score	0	0	1.7	1
Reversibility*)	-	-	c	c
Average time (days) for reversion	-	-	7	7

D Dulling of cornea

*) Reversibility: c. = completely reversible; n.c. = not completely reversible; n. = not reversible

Conclusion

As the mean average score for conjunctivae redness and conjunctival oedema (chemosis) are below 2 seen in all animals at the 24 to 72 h readings, which was completely reversible within 7 days, it is concluded SAN 420I (SA-12) technical does not warrant classification for eye irritation.

RMS evaluation	Re-evaluation of the previously submitted study with the technical substance SAN 420I containing Btk SA-12 revealed slight conjunctival irritation that was completely reversible within 7 days. No adverse effects were detected on iris or cornea. Thus, according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, SAN 420I (SA-12) technical does not warrant classification for eye irritation.
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New data 2016

In absence of data on the formulated product, evaluation of the eye irritating potential according to Annex I of Regulation (EC) No. 1272/2008 is applied.

Based on re-evaluation of the previously submitted study with SAN 420I (SA-12) technical it can be concluded that the active ingredient Btk SA-12 does not warrant classification for eye irritation according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.

Also the co-formulant contained in CoStar WG is not classified in this regard. Hence, according to Regulation (EC) No. 1272/2008 the product CoStar WG does not warrant classification for eye irritation. No hazard statement or signal word is required.

RMS conclusion	<p>Re-evaluation of the previously submitted study with the technical substance SAN 420I containing Btk SA-12 revealed slight conjunctival irritation that was completely reversible within 7 days. No adverse effects were detected on iris or cornea. Thus, according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, SAN 420I (SA-12) technical does not warrant classification for eye irritation. Also, the co-formulant contained in CoStar WG is not classified as being irritating to eyes.</p> <p>Article 40 of the Pesticides Regulation provides that testing on vertebrates shall be undertaken only as a last resort. The use of non-animal test methods and other risk assessment strategies should be promoted. Animal testing for the purposes of this Regulation should be minimised and tests on vertebrates should be undertaken as a last resort. Seen in this context the available data on the active substance from first approval of Btk SA-12 are considered acceptable to cover current requirements. Therefore, no new studies are required.</p> <p>Thus, CoStar WG does not require classification with regard to eye irritation according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.</p>
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B.6.2.3 Skin sensitisation

As CoStar WG was not the representative formulation for original approval of Btk SA-12, no data on the formulation have been submitted before.

New data 2016

According to Commission Regulation (EU) No 284/2013, the available methods for testing dermal sensitisation are not suitable for testing microorganisms. Therefore, no study with the Btk SA-12 formulation CoStar WG is presented.

Thus, CoStar WG does not warrant classification with regard to skin sensitisation according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. In addition, the applicant recommends to **not using the warning phrase “Contains *B. thuringiensis* subsp. *kurstaki*. Microorganisms may have the potential to provoke sensitising reactions”** for the following reasons:

- For microorganisms currently approved in the EU, positive reports on sensitisation are absent for bacterial species
- As there are no appropriate test methods, it is impossible to demonstrate absence of sensitisation potential and evaluators therefore strongly rely on published literature, where very little reports on sensitisation caused by species used for plant protection are found. Reports on sensitisation caused by microbials are mostly restricted to moulds, often in combination with moisture in buildings. On the other hand, non-pathogenic bacteria are considered to be able to protect human from sensitisation. This is also confirmed by the EFSA External report “Literature search and data collection on RA for human health for MO used as PPP” (Hackl et al. 2015)³.
- If exposure to microorganisms during use of plant protection products is compared to “natural” exposure in home or outdoor environments, plant protection products will hardly and only in rare cases exceed natural exposure.
- In other regulatory areas, microorganisms are not considered as potentially sensitising by default although exposure may considerably exceed the one in plant protection. Again, sensitisation is restricted

³ Evelyn Hackl, Margit Pacher-Zavisin, Laura Sedman, Stefan Arthaber, Ulla Bernkopf, Günter Brader, Markus Gorfer, Birgit Mitter, Aspasia Mitropoulou, Monika Schmoll, Willem van Hoesel, Elisabeth Wischnitzky, and Angela Sessitsch, 2015. Literature search and data collection on RA for human health for microorganisms used as plant protection products Reference. EFSA supporting publication 2015:EN-801. 173 pp.

to fungi, whereas bacteria and yeasts are considered to be beneficial with respect to human health (Martel et al., 2010).⁴

RMS conclusion	<p>According to Regulation (EC) 283/2013 (footnote 1 to point 5.2.1 in Part B), the available methods for testing dermal sensitisation are not suitable for testing microorganisms as microorganisms do not penetrate the skin.</p> <p>Currently no reliable, predictive <i>in vitro</i> or <i>in vivo</i> model exists for testing dermal or respiratory sensitisation of microorganisms.</p> <p>Thus, CoStar WG does not warrant classification with regard to skin sensitisation according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures. However, the following precautionary labelling phrase is currently required for all microorganisms in EU: “Contains <i>B. thuringiensis</i> subsp. <i>kurstaki</i>. Microorganisms may have the potential to provoke sensitising reactions”</p> <p>The RMS fully agree with the applicants argumentation and recommendation of not using the precautionary sentence for bacteria, yeast and virus approved as active substances under the Pesticides Regulation (EC) 1107/2009. However, the RMS considers it necessary to continue to use this precautionary sentence until otherwise agreed based on risk management in EU.</p>
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B.6.3 Data on exposure

The Microbial Pest Control Product CoStar WG containing the technical active ingredient *Bacillus thuringiensis* subsp. *kurstaki* SA-12 is intended to be used against tortricidae (*Cydia pomonella*) in pome fruits, against gelechiidae (*Tuta absoluta*) in solanaceous fruits, and against noctuid moths in ornamentals by professional and non-professional users.

CoStar WG is formulated as wettable granules, containing 850 g *Bacillus thuringiensis* subsp. *kurstaki* SA-12 per kg which correspond to a maximum of 5.7×10^{13} CFU/kg.

The maximum dose rate of CoStar WG is 1.5 kg/ha and 2.0 kg/ha in the field and 1.0 kg/ha in greenhouses. This corresponds to 1.2 kg and 1.7 kg active substance per ha, or 8.6×10^{13} CFU/ha and 1.1×10^{14} CFU/ha applied up to 6-times per growing season with a minimum interval of 7 days in the field. In greenhouses, this corresponds to 0.850 kg active substance or 5.7×10^{13} CFU/ha. The given data for the maximum application rates are listed in **Table 6.3-1**.

Table 6.3-1 Summary of critical Good Agricultural Practice for Delfin WG

Crop	Situation	Formulation Conc. of MPCA	Application		Application rate per treatment		
			Number (max.)	Interval between applications (min)	Kg a.s./ha	CFU/ha	Water L/ha [min - max]
Pome fruits (apple, pear)	Field	850 g/kg max. 5.7×10^{13} CFU/kg	6	7 days	1.275	8.6×10^{13}	1000 - 1500
Solanaceous fruits (tomato, aubergine, sweet pepper)	Greenhouse				0.85	5.7×10^{13}	200 - 1000
Ornamentals	Field				1.7	1.1×10^{14}	500 - 1000

⁴ Martel, Cyril; Nielsen, Gunnar D.; Mari, Adriano; Licht, Tine Rask; Poulsen, Lars Kærgaard. 2010. Bibliographic review on the potential of microorganisms, microbial products and enzymes to induce respiratory sensitization. EFSA supporting publication 2010 Volume 7, Issue 9, 95pp

Bacillus thuringiensis acts in a highly specific manner and is not pathogenic to mammals. This has been shown in many experimental studies on toxicity, pathogenicity, and infectiveness to vertebrates, all without adverse effects (Vol. 3 MA, B.6.1.4).

No harmful effects have been observed on personnel in research or industrial mass production, over a production period of more than 20 years (Document M-MA, Section 5, data point 5.1.2). Because inerts in the preparation are also of negligible toxicity, a toxic effect of CoStar WG on the operator, worker, or bystander can be excluded. For the same reasons no maximum allowable concentration (MAC) in drinking water was calculated.

Table 6.3-2: Product information and toxicological reference values used for safety assessment of pesticide application

Product name and code	CoStar
Formulation type	WG
Active substances (incl. content)	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> SA-12 850 g/kg (max. 5.7×10^{13} CFU/kg)
Category	Insecticide
Statement as to whether the product was already evaluated as the 'representative formulation' during the Annex I inclusion	CoStar WG was not the representative formulation for original approval of Btk SA-12, no data on the formulation have been submitted before.
AOEL systemic	Not applicable
Inhalative absorption	100%
Dermal absorption	0%

Estimation of operator exposure

Since no adverse effects were obtained in any study on toxicity, pathogenicity, or infectiveness, calculations on the health risk for operators become meaningless: no target organ exists and no dose-effect response (LOAEL) can be determined. Btk preparations including the Btk SA-12 preparation CoStar WG are considered safe for operators, bystanders and residents, and workers.

However, in order to meet the formal requirement to present an operator exposure assessment for the Btk preparation CoStar WG, calculations were compared to the NOAEL derived from an acute oral experimental study with the formulated product Thuricide ($LD_{50} > 5.4 \times 10^8$ CFU/animal, considering a body weight of 0.2 kg for a rat, this corresponds to 2.7×10^9 CFU/kg bw, **Table 6.6-1**) in rats and a margin of exposure was calculated. Thuricide is a liquid formulation of Btk SA-12.

Table 6.3-3 Parameters at GAP-use of CoStar WG (worst case scenario)

Crop/Use	Field or Glasshouse	Spraying Techniques	Work rate	Final volume L/ha	Application rate	Model
Pome fruits	Field	Vehicle mounted, upward spraying	10 ha/d	1000	1.275 kg a.s./ha 8.6×10^{13} CFU/ha	EFSA
Ornamentals	Field	Vehicle mounted, downward spraying	10 ha/d	500	1.7 kg a.s./ha 1.1×10^{14} CFU/ha	EFSA
		Hand-held sprayer	4 ha/d			
Fruiting vegetables	Greenhouse	Hand-held sprayer	1 ha/d	200	0.85 kg a.s./ha 5.7×10^{13} CFU/ha	IVA Dutch ECPA
	Indoor*		60 min/d			CRD

* Indoor use represents application by non-professional users

Theoretical exposure calculations according to the EFSA⁵ model are presented for field applications. For greenhouse applications, the IVA⁶, the Dutch⁷, and the ECPA⁸ model are used.

The models for professional use have no data for amateur users handling solid concentrate formulations. However, The CRD provided a model for amateur uses of plant protection products⁹. As a worst case the Trigger spray surface treatment model was employed assuming one hour of spraying.

Since the CFU are relevant for the biological effect, the application rate in weight (kg/ha/d) is used for the exposure estimation only (mg/kg bw/d) and then recalculated and expressed in CFU/kg bw/d using the worst case assumption of 6.7×10^7 CFU/mg Btk (5.7×10^{13} CFU/kg (active substance) in 850 g/kg (product) = 6.7×10^7 CFU/mg Btk). The given data for the maximum single application rates are listed in **Table 6.3-3**.

Btk SA-12 will not penetrate intact skin, as this is an effective barrier for microorganisms, thus external dermal exposure will not lead to systemic exposure. Therefore, no dermal absorption of the concentrate and the spray dilution is assumed. Moreover, inhalation exposure to Btk will be cleared by mucocilliary clearance mechanisms. During this process, oral ingestion is possible. Thus, in the worst case all inhaled micro-organisms are ingested.

Estimated operator exposures following field and greenhouse application of CoStar WG are summarized in **Table 6.3-4** and **6.3-5**, respectively.

For non-professional users, operator exposure is presented in **Table 6.3-6**.

⁵ EFSA (European Food Safety Authority), 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp.

⁶ Mich G, 1996. Operator exposure in greenhouse during practical use of plant protection product. Project EF 94-02-03; ECON Forschungs-und Bewertungskonzepte für Umwelt und Gesundheitssicherheit GmbH. Ingelheim. Unpublished.

⁷ Van Golstein Brouwers, Y.G.C., Marquart, J. and Van Hemmen, J.J. (1996). Assessment of occupational exposure to pesticides in agriculture. Part IV. Protocol for the use of generic exposure data. TNO Nutrition and Food Research Institute, The Netherlands. TNO Report V 96.120

⁸ European Crop Protection Association (ECPA) Southern European glasshouse model. Wicke, H. (2010) "Exposure to Pesticides in the Greenhouse: A new modelling approach in Europe", In: Non-Dietary Human Exposure and Risk Assessment, ACS Symposium Series, Vol. 1047, pp79-94.

⁹ http://www.pesticides.gov.uk/uploadedfiles/Web_Assets/PSD/Amateur%20use%20model2.xls

Table 6.3-4 Estimation of operator exposure to CoStar WG in the field to high and low crops for professional users, without PPE

Model data	Level of PPE	Work rate [ha/day]	Inhalation exposure [µg a.s./kg bw/day]		Total systemic exposure [mg/kg bw/day]	Total exposure a.s. [CFU/kg bw/day]	MoE*
			Mixing/ loading	Application			
Application with vehicle-mounted equipment outdoors to high crops, late season							
Application rate: 1.275 kg Btk SA-12/ha							
EFSA-Model 60 kg operator	None	10	1.33	4.48	0.006	4.0×10^5	6750
Application with vehicle-mounted equipment outdoors to low crops (ornamentals)							
Application rate: 1.7 kg Btk SA-12/ha							
EFSA-Model 60 kg operator	None	10	1.45	0.37	0.002	1.3×10^5	20769
Application with hand-held sprayer, outdoors to low crops (ornamentals)							
Application rate: 1.7 kg Btk SA-12/ha							
EFSA-Model 60 kg operator	None	4	1.10	1.96	0.003	2.0×10^5	13500

*MoE = NOAEL rat (2.7×10^9 CFU/ kg bw) per total exposure a.s. CFU/ kg bw/ day

Table 6.3-5 Estimation of operator exposure to CoStar WG in greenhouses for professional users, without PPE

Model data	Level of PPE	Inhalation exposure [µg a.s./kg bw/day]		Total systemic exposure [mg/kg bw/day]	Total exposure a.s. CFU/ kg bw/day	MoE*
		Mixing/ loading	Application			
Application rate: 0.85 kg Btk SA-12/ha, work rate: 1 ha/day						
IVA-Model, hand-held sprayer, high crops 70 kg operator	None	0.6	1.3	0.002	1.3×10^5	20769
Dutch model, Manual up- and downward spraying 70 kg operator	None	0.012		0.012	8.0×10^5	3375
ECPA model high crops (tomato) 1 ha/day 70 kg operator	None	0.166	8.23	0.008	5.4×10^5	5000

*MoE = NOAEL rat (2.7×10^9 CFU/ kg bw) per total exposure a.s. CFU/ kg bw/ day

As a worst-case scenario, vehicle-mounted application to high and low crops in the field or hand-held spraying to low crops in the field and in greenhouses were identified (Table 6.3-3). As presented in Table 6.3-4 and Ta-

ble 6.3-5, the estimated total operator exposure according to EFSA model without wearing PPE is 0.006 mg/kg bw/day corresponding to 4.0×10^5 CFU/kg bw/day when spraying CoStar WG by means of a tractor mounted device to high crops and 0.002 mg/kg bw/day corresponding to 1.3×10^5 CFU/kg bw/day when spraying to ornamentals. For orchards, this is 6750-times lower than the NOAEL derived from an acute oral toxicity studies in rats (**Table 6.6-1**), and 20800-times lower when spraying is performed to ornamentals. Hand-held spraying to low crops results in an estimated operator exposure of 2.0×10^5 CFU/kg bw/day, which is 13500-times lower than the NOAEL in rats.

For greenhouse use following hand-held spraying to high crops, the estimated total operator exposure according to IVA, Dutch, and ECPA model without wearing PPE is 0.002 mg/kg bw/day, 0.012 mg/kg bw/day, and 0.01 mg/kg bw/day, respectively. Thus, the estimated operator exposure is 3375- to 20800-times lower compared to the NOAEL.

Table 6.3-6 Estimation of operator exposure to CoStar WG to low crops, non-professional users, without PPE

Model data	Level of PPE	Work rate [h/d]	Inhalation exposure [mg/day]	Total systemic exposure [mg/kg bw/day]	Total exposure a.s. [CFU/ kg bw/ day]	MoE*
CRD-Model, hand-held sprayer, 60 kg operator	None	1	0.045	0.0007	4.7×10^4	57446

*MoE = NOAEL_{rat} (2.7×10^9 CFU/kg bw) per total exposure a.s. CFU/ kg bw/ day

RMS evaluation	<p>Since no adverse effects were obtained in any study on toxicity, pathogenicity, or infectiveness, calculations on the health risk for operators become meaningless: no target organ exists and no dose-effect response (LOAEL) can be determined. Btk preparations including the Btk SA-12 preparation CoStar WG are considered safe for operators, bystanders and residents, and workers.</p> <p>However, in order to meet the formal requirement the applicant has presented operator exposure assessments for the Btk preparation CoStar WG. Calculations were compared to the NOAEL derived from an acute oral experimental study with a liquid formulation of Btk SA-12 (2.7×10^9 CFU/ kg b.w., in rats and a margin of exposure calculated. It could be concluded: the preparation CoStar WG is considered safe for operators even without personal protective equipment for, both, professional and non-professional operators.</p> <p>The RMS are of the opinion that no quantitative exposure assessment is necessary since Btk SA-12 acts in a highly specific mode and is not pathogenic to mammals. This has been shown in many tests on toxicity, pathogenicity and infectiveness to vertebrates, all without adverse effects. Furthermore, no harmful effects have been observed on personnel in research or industrial mass production, over a production period of more than 20 years.</p> <p>Operator exposure may occur during mixing, loading and application. However, <i>Bacillus thuringiensis</i> will not penetrate intact skin, as this is an effective barrier for microorganisms. Thus, external skin exposure will not lead to systemic exposure and skin protection equipment is not necessary from a risk assessment point of view. CoStar WG are water dispersible granules and as such significant inhalation during mixing and loading is not expected. Therefore, given the use respiratory protection equipment (P284) is not considered necessary to address the potential for respiratory sensitization. In conclusion, exposure of operators to Btk SA-12, if even occurring, can be considered safe.</p>
Endpoint: Exposure of operator	A qualitative risk assessment for operators was performed. Comparison to no-effect levels demonstrates sufficient margins of exposure. No risk is anticipated.

Estimation of worker exposure

Worker exposure is considered negligible as dermal exposure is not relevant for Btk and inhalation exposure is not relevant for cultivation work or harvest.

RMS evaluation	<p>Worker exposure is considered negligible as dermal exposure is not relevant for Btk and inhalation exposure is not relevant for cultivation work or harvest. CoStar WG is not of toxicological concern for human health after dermal exposure. The qualitative risk assessment has shown that operators are not at risk when applying the product. Since dermal exposure is considered to be the most relevant route of exposure during crop maintenance and harvesting activities in the field and the intact skin is an effective barrier for microorganisms, worker exposure to <i>Bacillus thuringiensis</i> is considered to be negligible.</p> <p>Therefore, it is concluded that workers are not at risk when re-entering crops treated with CoStar WG. No re-entry period for handling treated product is necessary. In conclusion, exposure of workers to Btk SA-12, if even occurring, can be considered safe.</p>
Endpoint: Exposure of worker	No risk is anticipated.

Bystander and resident exposure

Resident exposure is not considered for application in greenhouses.

The maximum dose rate of CoStar WG is 2.0 kg /ha. This corresponds to 1.7 kg active substance per ha, or 8.6×10^{13} CFU/ha applied up to six times per growing season with a minimum interval of 7 days.

Considering a default distance of 10 m (orchards) and 2-3 m (low crops) to the field, dermal and inhalation exposure CoStar WG are considered to be negligible and not of specific concern.

However, as a conservative estimation, the EFSA model of resident exposure was applied for application in orchards (Table 6.3-7) and ornamentals (Table 6.3-8).

Btk will not penetrate intact skin, as this is an effective barrier for microorganisms, thus external dermal exposure will not lead to systemic exposure. Therefore, no dermal absorption is assumed. Moreover, the model considers default values for vapour which is considered to be not relevant for microorganisms. Inhalation exposure to Btk via spray drift or when entering treated crops will be cleared by mucocilliary clearance mechanisms. During this process, oral ingestion is possible. Thus, in the worst case all inhaled micro-organisms are ingested. For resident children also oral exposure (hand-to-mouth and object-to-mouth) of surface deposits is taken into consideration.

Table 6.3-7 Estimated resident exposure following broadcast air assisted application in orchards

Tractor mounted application to high crops		Resident	
		Child	Adult
total systemic exposure [µg a.s./kg bw/ day]	Spray drift (75 th percentile)	0.210	0.045
	Surface deposits (75 th percentile)	2.053	0.000
	All pathways (mean)	1.400	0.036
total systemic exposure [CFU/kg bw/ day]	All pathways (mean)	9.4×10^4	2.4×10^3
MoE*		2.8723×10^4	1.125×10^6

*MoE = NOAEL_{rat} (2.7×10^9 CFU kg b.w) per total exposure a.s. CFU/ kg bw/ day

Table 6.3-8 Estimated resident exposure following downward spraying to ornamentals

Tractor mounted application to low crops		Resident	
		Child	Adult
total systemic exposure [µg a.s./kg bw/ day]	Spray drift (75 th percentile)	0.075	0.006
	Surface deposits (75 th percentile)	5.741	0.000
	All pathways (mean)	4.261	0.005
total systemic exposure [CFU/kg bw/ day]	All pathways (mean)	2.9×10^5	335
MoE*		931	8.060×10^6

*MoE = NOAEL_{rat} (2.7×10^9 CFU kg b.w) per total exposure a.s. CFU/ kg bw/ day

Resident exposure for children following application of CoStar WG to orchards and low crops is calculated as 9.4×10^4 and 2.9×10^5 CFU per kg b.w. day, respectively. Thus, the estimated exposure is at least 930-times below the NOAEL derived from acute oral toxicity studies in rats. In adults, this exposure is even 1250000- and 8000000-times lower.

In conclusion, exposure of operators, workers, bystanders and residents to CoStar WG, if even occurring, can be considered safe even with the overly conservative approach.

RMS evaluation	<p>Since no adverse effects were obtained in any study on toxicity, pathogenicity, or infectiveness, calculations on the health risk for operators become meaningless: no target organ exists and no dose-effect response (LOAEL) can be determined. Bystander and resident exposure is lower than operator exposure since exposure during application will normally be very short. No significant volatilization is to be expected and bystander exposure will result primarily from drift. Thus, as concluded for operator exposure, CoStar WG does not represent a risk to human health. Hence it is concluded that bystanders and residents are also not at risk when applying the plant protection product according to Good Agricultural Practice.</p> <p>Btk preparations including the Btk SA-12 preparation CoStar WG are considered safe for operators, bystanders and residents, and workers.</p> <p>However, in order to meet the formal requirement, the applicant has presented a resident exposure assessment for the Btk preparation CoStar WG, calculations were compared to the NOAEL derived from an acute oral experimental study with the formulated product (2.7×10^9 CFU/ kg b.w., Point B.6.1.1) in rats and a margin of exposure calculated. Resident exposure for children is considered negligible as dermal exposure is not relevant for Btk and inhalation exposure to Btk via spray drift or when entering treated crops will be cleared by mucocilliary clearance mechanisms.</p>
Endpoint: Exposure of bystander	A qualitative risk assessment for operators was performed. Comparison to no-effect levels demonstrates sufficient margins of exposure. No risk is anticipated.

B.6.4 Available toxicological data relating to non-active substances

CoStar WG does not contain ingredients in concentrations of toxicologically critical concern. The properties of non-active ingredients and their toxicological data are provided in Volume 4, Safety Data Sheets for non-active substances.

B.6.5 Supplementary studies for combinations of plant protection products

CoStar Delfin WG is not intended for combinations with other adjuvants or pest control products. Furthermore, due to the nature of this biological insecticide, no influence on the toxicological profile of *Bacillus thuringiensis* is to be anticipated from interactions with chemical or other biological plant protection products.

B.6.6 References relied on

Please refer to point with References relied on in chapter B.6, in Volume 3 (MCPA) with regard to the evaluation of the literature search.

Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KMP 6.2.1/01	██████████	1999c	Costar technical concentrate – acute dermal irritation study in rabbits Certis USA LLC, Colombia ████████████████████ Report no. 5400-99 GLP: yes Published: no	yes	no	not protected	Certis USA	DAR 2008
KMP 6.2.2/01	██████████ ██████████	1992	Eye irritation to the rabbit of SAN 420I (SA-12) technical Certis USA LLC, Colombia ████████████████████ ████████████████████ Report no. 920159D/SNC 151/SE GLP: yes Published: no	yes	no	not protected	Certis USA	DAR 2008

Annex 1: Operator exposure

1.1 EFSA model: Operator exposure, vehicle mounted equipment, outdoor high crops, no PPE

Operator exposure for CoStar WG outdoor spray applications

Application rate of active substance		1.275 kg a.s./ha	<i>i_AppRate</i>		
Assumed area treated		10 ha/day	<i>d_AreaTreated</i>		
Amount of active substance applied		12.75 kg a.s./day	<i>i_AmountAS</i>		
Dermal absorption of the product		0.00%	<i>i_AbsorpProduct</i>		
Dermal absorption of in-use dilution		0.00%	<i>i_AbsorInuse</i>		
Formulation type		Wettable granules, soluble granules			
Indoor or Outdoor application		Outdoor			
Application method		Upward spraying			
Application equipment		Vehicle-mounted			
Season		late (dense foliage)			
OutdoorWettable granules, soluble granulesUpward sprayingVehicle-mounted					
Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	9303	45376	AOEM	
	Body	7392	33667	AOEM	
	Head	83	1142	AOEM	
	Protected hands (gloves)	87	401	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	178	793	AOEM	
	Protected head (hood and face shield)	1	65	AOEM	
	Inhalation	80	276	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	
Application	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
	Hands	24116	79519	AOEM	No data available for a drift reduction scenario
	Body	112349	655557	AOEM	
	Head	14765	90617	AOEM	
	Protected hands (gloves)	449	11723	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	1466	2865	AOEM	
	Inhalation	269	1054	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.35	0.35
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.006	0.006

1.2 EFSA model: Operator exposure, vehicle mounted equipment, outdoor to low crops, no PPE

Operator exposure for CoStar WG outdoor spray applications

Operator exposure for outdoor wettable granules/soluble granules spray applications					
Application rate of active substance		1.7 kg a.s./ha	i_AppRate		
Assumed area treated		10 ha/day	d_AreaTreated		
Amount of active substance applied		17 kg a.s./day	i_AmountAS		
Dermal absorption of the product		0.00%	i_AbsorpProduct		
Dermal absorption of in-use dilution		0.00%	i_AbsorInuse		
Formulation type		Wettable granules, soluble granules			
Indoor or Outdoor application		Outdoor			
Application method		Downward spraying			
Application equipment		Vehicle-mounted			
Season		not relevant			
Operator exposure for outdoor wettable granules/soluble granules spray applications					
Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	11610	56768	AOEM	
	Body	9049	36602	AOEM	
	Head	110	1522	AOEM	
	Protected hands (gloves)	105	535	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	229	1058	AOEM	
	Protected head (hood and face shield)	2	86	AOEM	
	Inhalation	87	278	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	
Application	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
	Hands	27546	29855	AOEM	This scenario assumes that small area equipment is used
	Body	37793	47889	AOEM	
	Head	226	2656	AOEM	
	Protected hands (gloves)	101	30	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	473	559	AOEM	
	Inhalation	22	206	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.11	0.11
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.002	0.002

1.3 IVA model: Operator exposure, Manual-hand held equipment, low crops, with and without PPE

EFSA model: Operator exposure, hand-held spray application outdoor to low crops, no PPE

Operator exposure for CoStar WG outdoor spray applications

Application rate of active substance		1.7 kg a.s./ha	i_AppRate		
Assumed area treated		4 ha/day	d_AreaTreated		
Amount of active substance applied		6.8 kg a.s./day	i_AmountAS		
Dermal absorption of the product		0.00%	i_AbsorpProduct		
Dermal absorption of in-use dilution		0.00%	i_AbsorInuse		
Formulation type		Wettable granules, soluble granules			
Indoor or Outdoor application		Outdoor			
Application method		Downward spraying			
Application equipment		Manual-Hand held			
Season		not relevant			
Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	5734	27813	AOEM	
	Body	4752	28047	AOEM	
	Head	44	609	AOEM	
	Protected hands (gloves)	58	214	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	102	423	AOEM	
	Protected head (hood and face shield)	1	34	AOEM	
	Inhalation	66	272	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
Water soluble bag	No		1		
Application	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
	Hands	6999	19099	AOEM	
	Body	402868	621098	AOEM	
	Head	54	385	AOEM	
	Protected hands (gloves)	23	100	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	40360	283923	AOEM	
	Inhalation	118	118	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.18	0.18
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.003	0.003

1.4 IVA model: Operator exposure, high crops, greenhouse use

IVA model handheld sprayer

Product CoStar WG

Active Ingredient g/L 850 *Bacillus thuringiensis* subsp. *kurstaki* strain SA-12

Crop Fruiting vegetables **Type of Formulation (liquid/WP/WG)** WG

Amount of water L/ha 200 **Dermal absorption mix/load %** 0

Maximum dosage L/ha 1 **Dermal absorption spraying %** 0

AOEL mg/kg bw/day n.a. **Inhalation absorption %** 100

Task	Type of exposure ¹	Specific exposure (mg/person x kg a.i.)	Work rate (ha/day)	Application rate (kg a.i./ha)	Estimated (mg/person/day)	exposure (mg/kg bw/day)
**Mix/load	I _M	0.05	1	0.8500	0.0425	0.00061
	D _{M(H)}	21	1	0.8500	17.8500	0.25500
***Application	I _A	0.11	1	0.8500	0.0935	0.00134
	D _{A(H)}	13.2	1	0.8500	11.2200	0.16029
	D _{A(C)}	1.56	1	0.8500	1.3260	0.01894
	D _{A(B)}	82.5	1	0.8500	70.1250	1.00179

¹ I_M Inhalation exposure during mixing/loading.

D_{A(H)} Dermal hand exposure during application.

D_{M(H)} Dermal hand exposure during mixing/loading.

D_{AC} Dermal head (capita) exposure during application.

I_A Inhalation exposure during application.

D_{A(B)} Dermal body exposure during application.

Route of exposure	Exposure	With protective equipment			
	Without protective equipment	Protective gloves			Protective Coverall
		during mixing	during application	during mixing and application	
Inhalation					
Mixing/loading		ST110	none	ST110	st110
	0.0006	0.000030	0.000607	0.000030	0.000030
Application		none	ST120	ST120	st120
	0.0013	0.001336	0.000067	0.000067	0.000067
Total inhalation:	0.001943	0.001366	0.000674	0.000097	0.000097
Dermal					
Mixing/loading		none	none	none	SS110
- Hands	0.2550	0.2550	0.2550	0.2550	0.0026
Application		none	none	none	SS120
- Hands	0.1603	0.1603	0.1603	0.1603	0.0016
		none	none	none	none
- Head	0.0189	0.0189	0.0189	0.0189	0.0189
		none	none	none	SS220
- Body	1.0018	1.0018	1.0018	1.0018	0.0501
Total dermal:	1.4360	1.4360	1.4360	1.4360	0.0732
Total systemic¹	0.0019	0.0014	0.0007	0.0001	0.0001

SS110 / SS120: universal protective gloves, factor 0.01

SS 210 / SS220: standard protective garment and sturdy footwear (e.g. rubber boots), factor: 0.05

SS 410 / 420: broad-brimmed headgear of sturdy fabric, factor: 0.5

SS 510 / 520: hood and visor, factor: 0.05

ST 110 / 120: particle filtering halfmask FF2-SL or half-mask (particle filter P2), factor: 0.8 (dermal) and 0.05

ST 210 / 220: halfmask with combination filter A1P2, factor: 0.8 (dermal) and 0.02 (inhalative)

¹ Assumes absorption dermal (%): 0 ; inhalative (%): 100

	Without protective equipment	With protective equipment/gloves			Full
		during mixing/loading only	during application only	during mixing/loading and application	during mixing/loading and
Exposure	0.0019	0.0014	0.0007	0.0001	0.0001

1.5 Dutch model: Operator exposure, high crops, greenhouse use

OPERATOR EXPOSURE		DUTCH GREENHOUSE MODEL	
form	CoStar WG	Application including mixing and loading	
a.s.	<i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> strain SA-12		
Parameter	Value	Unit	References, comments
MANUAL SPRAYING in greenhouses			
AR Application rate	0.85	kg a.s./ha	summary of intended uses
A Area treated	1	ha/ day	Dutch model
Inhalation Exposure			w ithout PPE
SV Surrogate Exposure Value	1	mg a.s./ kg a.s.	For dusting see note* (Dutch model)
Inhalation Exposure (w ithout PPE)	0.85	mg a.s./ day	IE = SV x AR x A
Inhalation Exposure (with PPE)			w ith PPE
PPE-factor	10		Non-pow ered mask filtertype 2 (most conservative): 10; more advanced RPE: see note** (Dutch model)
Inhalation Exposure (w ith PPE)	0.085	mg a.s./ day	IE(PPE) = (1/PPE factor) x IE
Dermal Exposure			w ithout PPE
SV Surrogate Exposure Value	200	mg a.s./ kg a.s.	For dusting see note* (Dutch model)
Dermal Exposure	170	mg a.s./ day	DE = SV x AR x A
Dermal Exposure (with PPE)			w ith PPE
PPE-factor	10		Gloves + coverall: 10 (Dutch model)
Dermal Exposure (w ith PPE)	17	mg a.s./ day	DE(PPE) = (1/PPE-factor) x DE
Internal exposure			
IA Inhalation Absorption	100	%	
DA Dermal Absorption	0	%	
AOEL		mg a.s./ day	based on 70 kg bw
		Without PPE	With PPE
Internal exposure	[mg a.s. / day]	[mg a.s. / day]	
Inhalation	0.8500	0.0850	IE(int) = IE x (IA/100)
Dermal	0.0000	0.0000	DE(int) = DE x (DA/100)
Total	0.8500	0.0850	sum
		% AOEL	
Inhalation	#DIV/0!	#DIV/0!	%AOEL = 100 x IE(int) / AOEL
Dermal	#DIV/0!	#DIV/0!	%AOEL = 100 x DE(int) / AOEL
Total	#DIV/0!	#DIV/0!	sum

1.6 ECPA model: Operator exposure, high crops, greenhouse use

ECPA Greenhouse model -Standard contact scenario						
Input Data		Bacillus thuringiensis subsp. kurstaki strain SA-12				
Product	CoStar WG			Maximum dosage L or kg/ha	1	
Active Ingredient g/L or kg	850			Type of Formulation	WG	
Crop	tomato			Dermal absorption (conc., %)	0	
Amount of water L/ha	200			Dermal absorption (spray, %)	0	
AOEL mg/kg bw/day				Inhalation absorption %	100	
Task	Type of exposure ¹	Specific exposure (mg/person/kg a.i.)	Work rate (ha/day)	Application rate (kg a.i./ha)	Estimated exposure (mg/person/ (mg/kg bw/day)	
Mixing/loading	I _M	0.0137	1	0.8500	0.0116	0.000166
	D _{M(H)}	2.29	1	0.8500	1.9465	0.027807
	D _{M(H)protected}	0.0297	1	0.8500	0.0252	0.000361
Application	I _A	0.678	1	0.8500	0.5763	0.00823
	D _{A(H)}	25.2	1	0.8500	21.4200	0.30600
	D _{A(C)}	0.806	1	0.8500	0.6851	0.00979
	D _{A(B)}	17.1	1	0.8500	14.5350	0.20764
FFP2 gloves hat uncertified coverall	I _A	0.054	1	0.8500	0.0459	0.00066
	D _{A(H)}	0.22	1	0.8500	0.1870	0.00267
	D _{A(C)}	0.322	1	0.8500	0.2737	0.00391
	D _{A(B)}	17.1	1	0.8500	14.5350	0.20764
¹ I _M Inhalation exposure during mixing/loading DM(H) Dermal hand exposure during mixing/loading I _A Inhalation exposure during application			D _{A(H)} Dermal hand exposure during application. D _{A(C)} Dermal head (capita) exposure during application. D _{A(B)} Dermal body exposure during application.			
Route of exposure	Exposure (mg/kg bw/day)					
	Without PPE	With protective gloves during mixing/ loading only		Additional protective measures for risk reduction		
Inhalation						
Mixing/loading	0.000166	none	0.000166	none	FFP2	0.000013
Application	0.008233	none	0.008233	none	FFP2	0.000656
Total inhalation:	0.008399		0.008399	0.008399		0.000669
Dermal						
Mixing/loading		SS110		gloves	gloves	
- Hands	0.0278	0.000361		0.000361	0.000361	
Application		none		gloves	gloves	
- Hands	0.3060	0.3060		0.0027	0.0027	
- Head	0.0098	0.0098		0.0098	0.0039	
uncertified coverall		uncertified coverall		uncertified coverall	uncertified coverall	
- Body	0.2076	0.2076		0.2076	0.2076	
Total dermal:	0.5512	0.5238		0.2205	0.2146	
Total systemic ¹	0.0084	0.0084		0.0084	0.0007	
² Assumes absorption dermal (%):		0	0 ; inhalative (%): 100			
	Without PPE	With protective gloves during mixing/ loading only		Additional protective measures for risk reduction		
Systemic operator exposure (mg/kg bw/day)	0.0084	0.0084		0.00840	0.00067	

1.7 CRD amateur use model

TRIGGER SPRAY SURFACE TREATMENT MODEL			
PRODUCT NAME	CoStar		
ACTIVE SUBSTANCE	Btk SA-12		
ACTIVE CONTENT	4.25 g/l		
DERMAL ABSORPTION	0 %		
AOEL	mg/kg bw/day		
	Rate of exposure ml/min	Exposure Duration (mins)	Estimated exposure to spray ml/day
Hand and forearm	0.0361	60	2.166
Legs, feet and face	0.0097		0.582
TOTAL DERMAL EXPOSURE TO SPRAY			2.748
ABSORPTION			0.0
ABSORBED DERMAL DOSE (mg/day)			0
	Rate of exposure ml/min	Exposure Duration (mins)	Estimated exposure to spray ml/day
Breathing rate = 1m ³ /h	0.000175	60	0.01050
INHALATION EXPOSURE - 100% ABSORPTION (mg/day)			0.044625
<div style="border: 1px solid black; padding: 10px; margin: 10px auto; width: fit-content;"> All data refer to the 75th percentile values </div>			
DERMAL (mg/day)	0		
INHALATION (mg/day)	0.044625		
TOTAL (mg/day)	0.044625		
BODYWEIGHT (kg)	60		
OPERATOR EXPOSURE (mg/kg bw/day)		0.0007438	

Annex 2: Resident exposure for field use according to the EFSA model

2.1 EFSA model: Residents exposure following application in orchards

Resident exposure for CoStar WG

Croptype	Pome fruit	
Application method	Upward spraying	
Application equipment	Vehicle-mounted	<i>i_AppEquip</i>
Formulation type	Wettable granules, soluble granules	<i>i_FormVal</i>
Buffer strip	10 m	<i>i_Buffer</i>
Application rate of the product	1.275 kg a.s./ha	<i>i_AppRate</i>
Concentration of active substance (in-use dilution for liquid applications)	1.275 g a.s./l	<i>d_ConcAS</i>
Dermal absorption of product	0.00%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	0.00%	<i>i_AbsorpInuse</i>
Oral absorption	100.00%	<i>i_AbsorpOrallnuse</i>
Dislodgeable foliar residue (<i>i_AppRate</i> * <i>i_DFR</i>)	3.825 µg a.s./cm ²	<i>d_DFR</i>
Vapour pressure of in-use dilution	low volatile substances having a vapour Pa pressure of <5*10-3Pa	<i>i_Volat</i>
Concentration in air	0.001 mg/m ³	<i>d_AirCon</i>
Resident dermal spray drift exposure 75th percentile - adult	5.63 ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	1.689 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00210 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00164 ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	3.68 ml spray dilution/person	
Resident dermal spray drift exposure mean - child	1.11 ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00170 ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00133 ml spray dilution/person	
Exposure duration dermal	2 hours	<i>d_ReExpDur</i>
Exposure duration inhalation	24 hours	<i>d_ReExpDurlnhal</i>
Exposure duration entry into treated crops	0.25 hours	<i>d_ExpDurTreatCrop</i>
Light clothing adjustment factor	18.0%	<i>d_ClothAF</i>
Breathing rate adult	0.23 m ³ /day/kg	<i>d_BreathRAd</i>
Breathing rate child (1-3 year old)	1.07 m ³ /day/kg	<i>d_BreathRCh</i>
Drift percentage on surface (75th percentile)	2.67%	
Drift percentage on surface (mean)	1.60%	
Turf transferable residues percentage	5.00%	<i>d_Turf</i>
Transfer coeff. of surface deposits-adult	7300 cm ² /hour	<i>d_ReTCAd</i>
Transfer coeff. of surface deposits-child (1-3 year old)	2600 cm ² /hour	<i>d_ReTCCCh</i>
Saliva extraction percentage	50.00%	<i>d_SalExt</i>
Surface area of hands mouthed	20 cm ²	<i>d_AreaHM</i>
Frequency of hand to mouth activity	9.5 events/hour	<i>d_ReFreqHM</i>
Ingestion rate for mouthing of grass per day	25 cm ²	<i>d_MouthGrass</i>
Dislodgeable residues percentage transferability for object to mouth	20.00%	<i>d_DRP</i>
Transfer coefficient for entry into treated crops (75th percentile) - a	7500 cm ² /h	<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (75th percentile) - cl	2250 cm ² /h	<i>d_TcEntryCh</i>
Transfer coefficient for entry into treated crops (mean) - adult	5980 cm ² /h	<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (mean) - child	1794 cm ² /h	<i>d_TcEntryCh</i>

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0002095	0.0010700	0.0020529	0.0000000	0.0024699

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0000446	0.0002300	0.0000000	0.0000000	0.0002661

2.2 EFSA model: Residents exposure following application in ornamentals

Resident exposure for CoStar WG

Croptype	Ornamentals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	<i>i_AppEquip</i>
Formulation type	Wettable granules, soluble granules	<i>i_FormVal</i>
Buffer strip	2-3 m	<i>i_Buffer</i>
Application rate of the product	1.7 kg a.s./ha	<i>i_AppRate</i>
Concentration of active substance (in-use dilution for liquid applications)	3.4 g a.s./l	<i>d_ConcAS</i>
Dermal absorption of product	0.00%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	0.00%	<i>i_AbsorpInuse</i>
Oral absorption	100.00%	<i>i_AbsorpOrallnuse</i>
Dislodgeable foliar residue (<i>i_AppRate</i> * <i>i_DFR</i>)	5.1 µg a.s./cm ²	<i>d_DFR</i>
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa	<i>i_Volat</i>
Concentration in air	0.001 mg/m ³	<i>d_AirCon</i>
Resident dermal spray drift exposure 75th percentile - adult	0.47 ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022 ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318 ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18 ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009 ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017 ml spray dilution/person	
Exposure duration dermal	2 hours	<i>d_ReExpDur</i>
Exposure duration inhalation	24 hours	<i>d_ReExpDurInhal</i>
Exposure duration entry into treated crops	0.25 hours	<i>d_ExpDurTreatCrop</i>
Light clothing adjustment factor	18.0%	<i>d_ClothAF</i>
Breathing rate adult	0.23 m ³ /day/kg	<i>d_BreathRAAd</i>
Breathing rate child (1-3 year old)	1.07 m ³ /day/kg	<i>d_BreathRCh</i>
Drift percentage on surface (75th percentile)	5.60%	
Drift percentage on surface (mean)	4.10%	
Turf transferable residues percentage	5.00%	<i>d_Turf</i>
Transfer coeff. of surface deposits-adult	7300 cm ² /hour	<i>d_ReTCAd</i>
Transfer coeff. of surface deposits-child (1-3 year old)	2600 cm ² /hour	<i>d_ReTCCh</i>
Saliva extraction percentage	50.00%	<i>d_SalExt</i>
Surface area of hands mouthed	20 cm ²	<i>d_AreaHM</i>
Frequency of hand to mouth activity	9.5 events/hour	<i>d_ReFreqHM</i>
Ingestion rate for mouthing of grass per day	25 cm ²	<i>d_MouthGrass</i>
Dislodgeable residues percentage transferability for object to mouth	20.00%	<i>d_DRP</i>
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500 cm ² /h	<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (75th percentile) - child	2250 cm ² /h	<i>d_TcEntryCh</i>
Transfer coefficient for entry into treated crops (mean) - adult	5980 cm ² /h	<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (mean) - child	1794 cm ² /h	<i>d_TcEntryCh</i>

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0000748	0.0010700	0.0057410	0.0000000	0.0053311

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0000057	0.0002300	0.0000000	0.0000000	0.0002351