European Commission

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

Spodoptera exigua multicapsid nucleopolyhedrovirus (SeMNPV)

Product data: SPEXIT

Volume 3 – Annex B.6 Toxicology

Rapporteur Member State: Spain

April 2020

Version History

When	What
18/09/2018	Completeness check report of the dossier submitted by the notifier
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April 2020	DAR updated after EFSA completeness check

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INTRODUCTION

This dossier is submitted by Andermatt Biocontrol GmbH, Switzerland, for the approval of *Spodoptera exigua* multicapsid nucleopolyhedrovirus (SeMNPV) and the formulated product SPEXIT to the European authorities for the evaluation of the microbial pest control agent under the Regulation (EC) 1107/2009 of European Parliament. SPEXIT is a microbial pest control product formulated as a suspension concentrate containing 3.75 x 10^{12} occlusion bodies (OB) of SeMNPV in 1.0 L product.

The intended target insect is the beet armyworm *Spodoptera exigua* in pepper and leafy vegetables (lettuce crops). For more details, please refer to **Table 6.1**.

SPEXIT 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.

Spodoptera exigua MNPV belongs to the family of baculoviruses. The use of data of other baculovirus species in this dossier is justifiable due to this family relationship. This virus acts highly specific and exclusively against larvae of the beet armyworm, *Spodoptera exigua* and is not supposed to have any harmful effects on organisms not belonging to the family of Noctuidae. With regard to safety considerations, it is important to note that SeMNPV and the whole group of baculoviruses are naturally present in the environment. The experience that baculoviruses present no risk to mammals, including humans has been confirmed by numerous studies. Their application in pest control means only a fluctuation of the virus titre in the biotope of the pest insect.

Active substances are approved for maximum period of 10 years under Directive 91/414/EEC[1]. The active substance SeMNPV was under programme of renewal Regulation EU 686/2012 (AIR-III programme[2]). According to draft working document AIR III renewal programme SANCO/2012/11284[3], *Spodoptera exigua* nuclear polyhedrosis virus was included in Batch 9" Active substance *Spodoptera exigua* nuclear polyhedrosis virus No application for renewal of approval has been submitted. Previous expiry date 30/11/2017"

Commission implementing regulation (EU) No 844/2012[4] setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 establishes in its Art 1: "the application for the renewal of an approval of an active substance shall be submitted by a producer of the active substance to the rapporteur Member State, no later than three years before the expiry of the approval"

The application for the renewal of the active substance *Spodoptera exigua* nuclear polyhedrosis virus was not submitted before of three years before the expiry date of the approval of the active substance SeMNPV (30/11/2017).

The applicant then have submitted an application for SeMNPV as a new active substance.

In this RAR, the information submitted regarding *Spodoptera exigua* multicapside nucleopopyhedrovirus (SeMNPV) is evaluated as new active substance, therefore, all information is considered and evaluated as new.

[1] *Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230 of 19.8.1991.C.*
[2] *Programme of renewal Regulation EU 686/2012 (AIR-III programme).*
[3] *SANCO/2012/11284 –rev. 22, December 2018. Draft working document AIR III renewal programme.*
[4] *Commission implementing regulation (EU) No 844/2012, of 18 September 2012. Setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.*

Table 6.1 GAP table: Details of all national gaps within each zone

MPCP/PPP (product name/code) **SPEXIT** **Formulation:** **Type:** **SC**
MPCA: active ingredient **Spodoptera exigua multicapsid nucleopolyhedrovirus (SeMNPV)** **Conc. of a.s :** 3.75×10^{12} OBs/L

Zone(s): **EU** **Professional use** ☒ **Non professional use** ☒

1	2	3	4	5	7	8	9	10	11	12	13	14
Use-No	**Member state(s)**	**Crop and/ or situation** (crop destination/purpose of crop) (c)	**F G or I** (d)	**Pests or Group of pests controlled** Additionally: developmental stages of the pest or pest group (e)	**Application** Method Kind (f-g)	**Application** Timing/ Growth stage of crop & season (h)	**Application** Max number (min interval between applications) a) per use b) per crop/ season	**Application rate per treatment** L product /ha a) max rate per appl. b) max. total rate per crop/season (i)	**Application rate per treatment** OBs /ha a) max rate per appl. b) max. total rate per crop/season	**Application rate per treatment** Water L/ha min/ max	**PHI (days)** (j)	**Remarks** e.g. g. safener/synergist per ha (k)
1	EU	Pepper (CPSAN)	F/G	*Spodoptera exigua* (LAPHEG)	Spray	At infestation (preferably on early larva instar: L1 and L2). First treatment just before hatching)	a) 18 (6) b) 18 (6)	a) 0.2 b) 3.6	a) 7.5×10^{11} b) 1.35×10^{13}	200 / 1600	-	- 2 to 3 applications per pest generation, up to 6 generations. -Interval between applications: min. of 6 sunny days; 2 partially sunny days = 1 sunny day
2	EU	Leafy vegetables (lettuce crops) (3LETC)	F/G	*Spodoptera exigua* (LAPHEG)	Spray	At infestation (preferably on early larva instar: L1 and L2). First treatment just before hatching)	a) 18 (6) b) 18 (6)	a) 0.2 b) 3.6	a) 7.5×10^{11} b) 1.35×10^{13}	200 / 1600	-	- 2 to 3 applications per pest generation, up to 6 generations. -Interval between applications: min. of 6 sunny days; 2 partially sunny days = 1 sunny day

Remarks:

a) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR).
b) GCPF Codes - GIFAP Technical Monograph No 2, 1989.
c) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure).
d) Outdoor or field use (F), glasshouse application (G) or indoor application (I).
e) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds.
f) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench.
g) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.
h) Growth stage at last treatment (BBCH Monograph, Growth stages of mono-and dicotyledonous plants, 2º edit 2001, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application.
i) The minimum and maximum number of application possible under practical conditions of use must be provided.
j) PHI - minimum pre-harvest interval.
k) Remarks may include: Extent of use/economic importance/restrictions.

B.6. EFFECTS ON HUMAN HEALTH

Studies performed with the product Granupom (containing 2.2×10^{13} OB/L *Cydia pomonella* granulovirus, CpGV) or with other baculovirus preparations could be considered applicable and relevant also with regard to the evaluation of the formulated product SPEXIT. GRANUPOM (or Granulosevirus CpGV SC) contains the same co-formulants as SPEXIT. Therefore, studies conducted with GRANUPOM (or Granulosevirus CpGV SC) could be applicable to assess possible effects of SPEXIT. Risk assessment for SPEXIT with the proposed use pattern is provided here and is considered adequate with regard to the evaluation of effects on non-target arthropods, other than bees, of the formulated product. However, as in the evaluation of the substance, studies are considered additional information.

B.6.1. BASIC ACUTE TOXICITY STUDIES

Baculoviruses isolated from a certain host are infectious only for insects of the same order (Lepidoptera) and mostly even of the same family the original host belongs to. SeMNPV multiplies only in few species of the family *Noctuidae* (Gröner, 1986). Because of this high host specificity and the lack of pathogenicity or infectivity to other organisms of SeMNPV and of baculoviruses in general it is appropriate to include all results of baculovirus toxicity as being relevant also for SeMNPV/SPEXIT (Gröner, 1990).

RMS comments and conclusion

According to the OECD Consensus Document (ENV / JM / MONO (2002) 1), baculovirus species are extremely host-specific and only occur in arthropods. Baculoviruses are not infective for mammals and replication does not occur in mammalian cells.

B.6.1.1. Acute oral toxicity

No study assessing the effect of the microbial pest control product SPEXIT on human health is submitted here. No signs of toxicity, pathogenicity or infectivity have been detected upon acute oral exposure to baculoviruses.

SPEXIT 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.

Thus, SPEXIT 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 comments and conclusion

The studies presented for the evaluation of the oral acute toxicity were performed with baculoviruses other than SeMNPV. In addition, these studies were not carried out with a formulation similar to the product notified by the applicant, but with a suspension of the baculovirus diluted with water, and also we do not have the composition certificate of the formulation. Signs of toxicity, pathogenicity or infectivity have not been evaluated, this is considered a DATA GAP. Although SPEXIT could be considered Unclassified according to Regulation 1272/2008 criteria, the active substance is a microorganism and therefore the criteria for chemicals classification does not apply.

B.6.1.2. Acute inhalation toxicity

No study assessing the effect of the microbial pest control product SPEXIT on human health is submitted here.

SPEXIT 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.

SPEXIT 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 comments and conclusion

The applicant has not presented studies that evaluate the acute inhalation toxicity, only information regarding respiratory sensitization for baculoviruses that are not the virus notified by the applicant that was submitted for the evaluation of the active substance(Section B.6, Point B.6.1.2.2.2/01). This study is not adequate for the evaluation of acute inhalation toxicity because the doses tested are lower than the limit test dose level and very short times of exposure (5-15 min) were performed. This should be considered a DATA GAP. Although SPEXIT could be considered unclassified according to Regulation 1272/2008 criteria, the active substance is a microorganism and therefore the criteria for chemicals classification does not apply.

B.6.1.3. Acute percutaneous toxicity

Microorganisms do not penetrate intact human skin. Hence, no study on dermal toxicity was performed with the SeMNPV nor with the formulated product SPEXIT. Also none of the co-formulants of SPEXIT is of toxicologically critical concern with regard to dermal toxicity. The properties of non-active ingredients and their toxicological data are provided in Volume 4.

Thus, SPEXIT 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 comments and conclusion

The applicant states that baculoviruses do not penetrate human skin. The non-submission of an acute percutaneous toxicity study is acceptable. Although SPEXIT could be considered unclassified according to Regulation 1272/2008 criteria, the active substance is a microorganism and therefore the criteria for chemicals classification does not apply.

B.6.2. ADDITIONAL ACUTE TOXICITY STUDIES

B.6.2.1. Skin irritation

Reference	[redacted] (1998)
Study	Acute dermal irritation/corrosion; Granupom SC (CpGV); [redacted] Unpublished report no. 981042829
Guidelines	OECD 404
Deviations	No
GLP	Yes
Acceptability	Yes

Materials and Methods

Test substance	Granupom SC (CpGV: 2.2×10^{13} granules/L)
Test animals	3 Albino rabbits (all male)
Method	The test substance was applied undiluted dermally in a single dose of 0.5 mL/animal onto the shaved dorso-lumber region of 3 rabbits. The application site was covered with a patch (width 6 cm) and secured by an occlusive bandage (width 8 cm). After removal of the bandage at the end of the exposure period (4 h) the residual test substance was gently removed with water. Observations on mortality, behaviour, clinical signs, body weight, and skin reactions.

Results and Conclusion

A. Results

During the observation period of 10 days no mortalities and no systemic toxicological symptoms were noted. The behaviour was inconspicuous. The body weight gain was in the normal range. No signs of skin irritation were found after the 4 h-exposure period. Granupom does not produce any dermal irritation on the rabbit.

B. Conclusion

Granupom is not a dermal irritant and does not require classification.

No study with the product has been conducted. It is referred to a dermal irritation study following OECD TG 404 with Granupom revealing no skin irritating properties. Granupom contains the same co-formulations as SPEXIT (please refer to Confidential information).Thus, studies conducted with Granupom are fully applicable to assess possible effects of SPEXIT.

Similar results were obtained with rhesus monkeys which received a single subcutaneous injection of 10^8 PIB of *Heliothis* NPV (Ignoffo et al., 1975). For further details, please refer to Volume 3, Section B.6, Point B.6.2.1 Furthermore, SPEXIT does not contain additives of toxicological concern.

It is concluded that dermal applications of SPEXIT to the intact skin of mammals are not expected to cause clinical signs of systemic toxicity. Therefore, it can be concluded that SPEXIT is not irritating to the skin and does not require classification as a skin irritant 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 comments and conclusions

This study was not carried out with the formulated product SPEXIT but with a formulation called Granupom SC (CpGV). The applicant states that the coformulants of both products are the same. The RMS has been able to verify that this is true although they are in different concentrations. Therefore the equivalence of studies carried out with Granupom is accepted. Although SPEXIT could be considered Unclassified according to Regulation 1272/2008 criteria, the active substance is a microorganism and therefore the criteria for chemicals classification does not apply.

B.6.2.2. Eye irritation

Reference	[redacted] (1993)
Study	HOE 083311; water miscible suspension concentrate, 2.2×10^{13} vir/mL: (Code: Hoe 08331100 SC 13 A 401), Testing for primary eye irritation to the rabbit. [redacted] Unpublished report no. 93.0567
Guidelines	OECD 405 (Feb. 1987)
Deviations	No
GLP	Yes
Acceptability	Yes

Materials and Methods

Test substance	Granupom SC (CpGV: 2.2×10^{13} granules/L (batch no. Hoe 083311 00 SC 13 A 401)
Test animals	White rabbits
Method	0.1 mL Granupom was applied once to the conjunctival sac of the left eye of 3 rabbits. The untreated right eye served as a control. After an exposure time of 24 hours, the treated

	eyes were thoroughly washed out with physiological saline. The eyes were examined for ocular lesions at 1, 24, 48 and 72 hours, and 7 days after treatment.

Results and Conclusion

A. Results

No corneal opacity or iritis were observed. The overall average scores (24, 48, 72 hours) for conjunctival redness, chemosis and discharge were 1.33, 0.22 and 0.00, respectively. All signs of irritation were completely reversible within 7 days (**Table B.6.2.2-1**).

Table B.6.2.2-1 Eye irritation: scores according to the Draize Scheme (Granupom)

Time [h]		Cornea			Iris			Conjunctiva								
								Redness			Chemosis			Discharge		
	Animal #	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
1		0	0	0	0	0	0	1	2	1	1	1	1	2	1	1
24		0	0	0	0	0	0	1	2	2	0	1	0	0	0	0
48		0	0	0	0	0	0	1	2	2	0	1	0	0	0	0
72		0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
168		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean scores 24 - 72 h		0	0	0	0	0	0	0.66	1.66	1.66	0	0.66	0	0	0	0
Mean scores 24 - 72 h		0.00			0.00			1.33			0.22			0.00		

Irritation was scored according to Draize.

Granupom is only slightly irritating to the eyes and does not require classification.

B. Conclusion:

Based on reactions observed (mean eye irritation scores 24 to 72 hours after instillation of the test substance), Granupom is not an eye irritant.
No study on eye irritation has been performed with the formulated product SPEXIT. It is referred to an eye irritation study following OECD TG 405 with Granupom revealing only slightly eye irritating properties. Granupom contains the same co-formulations as SPEXIT. Thus, studies conducted with Granupom are fully applicable to assess possible effects of SPEXIT

Therefore, SPEXIT is only slightly irritating to the eyes and does not require classification as an eye irritant according to the Regulation (EC) No 1272/2008. No hazard statement or signal word is required.

RMS comments and conclusions
This study was not carried out with the formulated product SPEXIT but with a formulation called Granupom SC (CpGV). The applicant states that the coformulants of both products are the same. The RMS has been able to verify that this is true although they are in different concentrations. Therefore the equivalence of studies carried out with Granupom is accepted. Although SPEXIT could be considered Unclassified according to Regulation 1272/2008 criteria, the active substance is a microorganism and therefore the criteria for chemicals classification does not apply.

B.6.2.3. Skin sensitisation

No study assessing the effect of the microbial pest control product SPEXIT on human health is submitted here. It is referred to the information submitted for the active substance SeMNPV.

SPEXIT does not contain ingredients in concentrations of toxicologically critical concern. The properties of non active ingredients and their toxicological data are provide as confidential information.

According to Regulation (EC) No 283/2013, the available methods for testing dermal sensitisation are not suitable for testing microorganisms as microorganisms do not penetrate the skin. However, a study with baculovirus formulation Granupom containing the active substance CpGV was submitted in Volume 3, Section B6.1.2.1 (evaluation of the active substance). Granupom contains the same co-formulations as SPEXIT, and did not show any evidence for skin sensitising properties. Moreover, due to the high conformity of SeMNPV isolates and their specific mode of action, studies conducted with Granupom are fully applicable to assess possible effects of SPEXIT.

According to Regulation (EC) 283/2013 (foot note 1 to point 5.2.1 in Part B), the available methods for testing dermal sensitisation are not suitable for testing microorganisms as they do not penetrate the skin. Therefore, all microorganisms need to be labelled with a warning phrase "Microorganisms may have the potential to provoke sensitizing reactions". However, this phrase is not justified for viruses like SeMNPV for the following reasons:

- Viruses do not produce metabolites which might be sensitising.
- No signs of sensitisation or allergenicity have been reported in an occupational health report since 2006 (B6.1.1.2-01). There are no published reports on sensitisation induced by SeMNPV.
- Generally, for viral species currently approved in the EU, positive reports on sensitisation are absent.
- As there are no appropriate test methods, it is impossible to demonstrate absence of sensitisation potential. 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. This is also confirmed by the EFSA External report "Literature search and data collection on risk assessment for human health for microorganisms used as plant protection products" (Hackl et al. 2015) and a review by Martel et al (2010).

Thus, SPEXIT 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.

RMS comments and conclusions

The applicant states that Granupom contains the same co-formulants as SPEXIT. Although the applicant presents of number of reasons why virus should not be considered sensitizers, following the Regulation (EC) 283/2013, all microorganisms should be considered potential sensitizers.

B.6.3. DATA ON EXPOSURE

The Microbial Pest Control Product SPEXIT containing the technical active ingredient *Spodoptera exigua* multicapsid nucleopolyhedrovirus (SeMNPV) is intended to be used for treatment against the beet armyworm on pepper and leafy vegetables in the field and in greenhouses by professional users and by non-professional users.

SPEXIT is formulated as suspension concentrate, containing 3.75×10^{12} viable granules of SeMNPV in 1 L product.

The maximum single dose rate is 0.2 L/ha, corresponding to 7.5×10^{11} OB/ha in the field and in home gardens applied as foliar spray up to 18-times per growing season with a minimum interval of 6 days depending on the number of sunny days. The given data for the maximum application rates are listed in **Table B.6.1.**

Spodoptera exigua MNPV, like all baculoviruses, acts highly arthropod specific. No harmful effects have been observed on personnel in research or industrial mass production. Because inert formulants of the preparation are of negligible toxicity as well in the concentration used, a toxic effect of SPEXIT on the operator, worker, or bystander can be excluded. For the same reason, no maximum allowable concentration (MAC) in drinking water was calculated.

No harmful effects have been observed on personnel in research or industrial mass production, over the whole production period of more than 10 years (Andermatt 2006).

Table B.6.3.1 Product information and toxicological reference values used for safety assessment of pesticide application

Product name and code	SPEXIT
Formulation type	SC
Active substances (incl. content)	*Spodoptera exigua* multicapsid nucleopolyhedrovirus (SeMNPV) 3.75×10^{12} OB SeMNPV/L
Category	Insecticide
AOEL systemic	Not applicable
Inhalative absorption	100 %
Dermal absorption	10% for the concentrate and 50% for the diluted product*

*Default values according EFSA Guidance on Dermal absorption, 2017

Estimation of operator exposure

Since an AOEL has not been established at Community level for the active substance, there is no parameter to calculate the exposure, so the risk assessment has not been performed.

Estimation of worker exposure

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

Estimation of bystander and resident exposure

Following the above given reasons for abstaining from an estimation of operator risk assessment, this also applies with regard to bystanders. Baculovirus preparations including the SeMNPV preparation SPEXIT are considered safe for bystanders as well.

No hypersensitivity incidents were reported for personnel involved in production of SPEXIT (SeMNPV) and other baculovirus products (Andermatt, 2006).

The maximum dose rate of SPEXIT is 0.2 L/ha. This corresponds to 0.104 kg active substance per ha, or 7.5×10^{11} OB/ha applied up to eighteen times per growing season with a minimum interval of 6 days.

RMS comments and conclusions

ADI, ARfD and AOEL are not necessary (and not possible to be derived based on the available data) due to the low toxicological concern related to baculoviruses, so the risk assessment has not been performed.

Nevertheless, the applicant has included estimation of exposure of professional and amateur users. Some errors have been detected in these estimations. The NOAEL employed derived from an acute oral toxicity study with AcNPV in rats not with CpGV. In addition 7.5×10^8 is the number of OB of AcNV/animal that corresponds with 5×10^9 OB AcNV/kg bw assuming a body weight of 150 g.

The product is diluted in water prior to application. The product concentrate is added to an appropriate amount of water before its application using a vehicle mounted spraying equipment, a hand-held sprayer or a knapsack sprayer. There is a potential for accidental skin exposure during mixing and loading activities, therefore the use of suitable protective clothing (coveralls and gloves) is recommended. Since the product is a suspension concentrate, the generation of particles or aerosols of inhalable size is not expected during the mixing and loading. The application of SPEXIT using a hand-held sprayer may result in dermal contamination from spray drift and directly from spraying equipment; therefore the use of suitable protective clothing (coveralls and gloves) is recommended. Spray application may also generate particles of inhalable size, therefore the additional use of respiratory protective equipment is recommended.

As the product contains microorganisms as active substances, the use of PPE is recommended as a precautionary measure:

- *Chemical protection gloves.*
- *At least, type 6 splash proof protection clothes.*
- *Respiratory protection: At least, level FFP2 self-filtering mask for particles or level P2 filtering mask.*
- *Chemical proof footwear*

B.6.4. AVAILABLE TOXICOLOGICAL DATA RELATING TO NON-ACTIVE SUBSTANCES

SPEXIT does not contain ingredients of toxicological concern.

B.6.5. SUPPLEMENTARY STUDIES FOR COMBINATIONS OF PLANT PROTECTION PRODUCTS

No studies for combinations of plant protection products have been carried out.

B.6.6. SUMMARY AND EVALUATION OF HEALTH EFFECTS

All submitted toxicological studies on baculoviruses and supplemental information on SeMNPV, prove that these highly arthropod-specific viruses are non-infectious to mammals and impose no health risk for operators, workers and bystanders. As SPEXIT does not contain any co-formulants requiring classification and labelling towards health hazard, it is justified to expect that also the microbial pest control product does not impose any risks to the health of humans or mammals.

Microorganisms do not penetrate intact skin. Additionally, the study conducted with Granupom, which contains the same co-formulants as SPEXIT, did not show any evidence for skin sensitising properties. The co-formulants of the preparation SPEXIT, formulated as suspension concentrate, are inert and no hazards to the human health are expected

Thus, according to the Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, SPEXIT does not require classification on the basis of acute toxicity testing. No hazard statement or signal word is required.

RMS comments and conclusions
Despite the results on the sensitization study commented on by the applicant, according to Regulation (EC) 283/2013, all microorganisms should be regarded as potencial sensitisers.

Although SPEXIT could be considered unclassified according to Regulation 1272/2008 criteria, the active substance is a microorganism and therefore the criteria for chemicals classification does not apply.

Table B.6.6.1 Summary of acute toxicity studies on Baculovirus products

Study type	Test item	Dose level	Findings	Report
Acute oral toxicity rat	AcNPV	5×10^9 PIB /kg bw	No adverse effect This is considered additional information.	[redacted] (1980)
Respiratory sensitisation guinea pig	CpGV, HOE 083311; water miscible suspension concentrate (product Granupom), 2.2 x 10^{13} vir/L:	35 mg (7×10^8 granules) per m^3	There is not method. This is considered additional information.	[redacted] (1992)
Dermal irritation rabbit	Granupom (CpGV)	0.5 mL /animal	Non-irritating	[redacted] (1998)
Eye irritation/ infectivity rabbit	CpGV, HOE 083311; water miscible suspension concentrate (product Granupom), 2.2 x 10^{13} vir/mL	0.1 mL	Non-irritating	[redacted] (1993)
Skin sensitisation Landsteiner guinea pig	CpGV, HOE 083311 OI LC08 A101(product Granupom)	0.1 mL	According to Regulation (EC) 283/2013, all microorganisms should be regarded as potencial sensitisers.	[redacted] (1986)

B.6.7. REFERENCES RELIED ON

Reference list (ABA - Andermatt Biocontrol)

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
B.6.1/01	Gröner, A.	1986	Specifity and safety of baculoviruses. The Biology of Baculoviruses, Biological Properties and Molecular Biology, Publisher: CRC Press, 9, 177 - 201 No GLP Published	N	N		-
B.6.1/02	Gröner, A.	1990	Cydia pomonella granulosis virus (CpGv) Hoe 083311 Summary and conclusions on the toxicity Andermatt Biocontrol AG, CH, AgrEvo, Hoechst and Schering, Marburg, Germany No GLP Not Published	N	N	Proprietary information	ABA

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
B.6.2.1/01	[redacted]	1998	Acute dermal irritation /corrosion Granumpom SC (CpGv). Report 98 10 42 829 Andermatt Biocontrol GmbH, [redacted] GLP Not Published	Y	N	Proprietary information	ABA
B.6.2.1/02	Ignoffo, C.M., et al	1975	Insusceptibility of the Rhesus Monkey, *Macaca mulatta,* to an Insect Virus *Baculovirus heliothis* Environ Entomol, 4, 569 - 573 No GLP Not Published	Y	N		-
B.6.2.2/01	[redacted]	1993	Hoe083311Watermiscible suspension concentrate 2.2*10 exp13Vir/ml (Code Hoe 083311 00 SC13 A401)Testing for primary eye irritation in the rabbit. Report No. 93.0567, Study No. 93.0485 Andermatt Biocontrol AG, CH, [redacted] GLP Not Published	Y	N	Proprietary information	ABA
B.6.2.3/01	Hack,E et al..	2015	Literature search and data collection on risk assessment for human health for microorganisms used as plant protection products reference. EFSA supporting publication 2015:EN-801. 173 pp.	N	N		
B.6.2.3/02	Martel et al	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 Published	N	N		
B.6.3/01	Andermatt, M.	2006	Statement on the production of baculovirus products of Andermatt Biocontrol AG and on its workers exposure taking account of potential risks of inhalation toxicity Andermatt Biocontrol AG, CH, No GLP Not Published	N	Y	Proprietary information	ABA
B6.6/01	[redacted]	1980	Tolerance testing of AcNPV nuclear polyhedrosis virus following single-dose administration to SPF Wistar rats, Report No. 234/80 Andermatt Biocontrol AG, CH, [redacted] GLP Not Published	N	N	Proprietary information	ABA

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
B6.6/02	Ignoffo, C.M., et al	1975	Insusceptibility of the Rhesus Monkey, *Macaca mulatta*, to an insect virus, *Baculovirus heliothis* Environ Entomol, 4, 569 - 573 Not GLP Published	Y	N		-
B6.6/03	[redacted]	1992	Hoe 083311; water miscible suspension concentrate: 2.2*10 exp. 13 vir./1 (code: Hoe 083311 00 SC13 A102) testing for respiratory sensitization in the male and female Pirbright White guinea pig, Report No. 91.1096 Andermatt Biocontrol AG, CH, [redacted] GLP Not Published	Y	N	Proprietary information	ABA
B.6.6/04	[redacted]	1998	Acute dermal irritation/corrosion Granumpom SC (CpGv) Report 98 10 42 829 Andermatt Biocontrol AG, CH, [redacted] GLP Not Published	N	N	Proprietary information	ABA
B6.6/05	[redacted]	1993	Hoe 083311; water miscible suspension concentrate; 2.2*10 exp. 13 vir./ml (code: Hoe 083311 00 SC13 A401) Testing for primary eye irritation in the rabbit Report No.: 93.0485, 93.0567 Andermatt Biocontrol AG, CH, [redacted] GLP Not Published	Y	N	Proprietary information	ABA
B6.6/06	[redacted]	1986	Hoe 083311 OI LC08 A101 Testing for sensitising properties of Pirbright-White guinea pigs by the method of LANDSTEINER, Report No. 86.1373 Andermatt Biocontrol AG, CH, [redacted] GLP Not Published	N	N	Proprietary information	ABA