Renewal Assessment Report

Cydia pomonella GV

Volume 3 – B.9 Effects on non-target organisms

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Version history

When	What
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The RMS is the author of the Assessment Report. The Assessment Report is based on the validation by the RMS, and the verification during the EFSA peer-review process, of the information submitted by the Applicant in the dossier, including the Applicant's assessments provided in the summary dossier. As a consequence, data and information including assessments and conclusions, validated and verified by the RMS experts, may be taken from the applicant's (summary) dossier and included as such or adapted/modified by the RMS in the Assessment Report. For reasons of efficiency, the Assessment Report should include the information validated/verified by the RMS, without detailing which elements have been taken or modified from the Applicant's assessment. As the Applicant's summary dossier is published, the experts, interested parties, and the public may compare both documents for getting details on which elements of the Applicant's dossier have been validated/verified and which ones have been modified by the RMS.

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B.9 Effects on non-target organisms

Introduction

The companies Andermatt Biocontrol GmbH, Arysta Life Science S.A.S. and Serbios srl have agreed on the formation of a Task Force in order to submit a dossier for the renewal of approval of the micro-organism *Cydia pomonella* Granulovirus (CpGV) as an active substance in compliance with Regulation (EU) No 844/2012 and Regulation (EC) No 1107/2009.
The initial dossiers for inclusion of *Cydia pomonella* Granulovirus into Annex I of Commission Directive 91/414 were submitted to the authorities of Germany as rapporteur member state in November 2005. Andermatt Biocontrol GmbH and Probis GmbH together as a Task Force, Arysta LifeSience S.A.S. and Sipcam S.p.A were the notifiers in the initial evaluation of approval of CpGV as active substance. Serbios srl has acquired all data and registrations concerning CpGV and formulated products from Sipcam S.p.A..
Inclusion of the first isolate of *Cydia pomonella* Granulovirus (Mexican isolate) into Annex I (now list of approved active substances) entered into force on 01 May 2009 (Commission Directive 2008/113/EC[1]). This active substance is an approved active substance under Regulation (EC) 1107/2009 (repealing Commission Directive 91/414/EEC) as specified in Commission Implementing Regulation (EU) 540/2011 of 25 May 2011 and Commission Implementation Regulation (EU) No 880/2014 amending Commission Implementation Regulation (EU) No 540/2011. Further isolates were added to Annex I following evaluation according to the "Guidance Document SANCO/0253/2008 rev. 2 on the assessment of new isolates of baculovirus species already included in Annex I of Council Directive 91/414" in May 2011, when the SCFCAH took note of the amended review report of 5 May 2011.
The dossier comprised the following isolates: the Mexican isolate CpGV-M, CpGV-15, CpGV-22, CpGV-V03, CpGV-V01 and CpGV-R5.
Cydia pomonella Granulovirus (CpGV) belongs to the group of baculoviruses. The inclusion of data from other baculoviruses is deemed justified due to this group relationship and close similarity of all baculoviruses in terms of their biology. Baculoviruses and CpGV in particular have been used for decades as plant protection products to control diverse pest insects. CpGV acts highly specific against larvae of the codling moth, *Cydia pomonella* and some isolates can infest the Oriental fruit moth *Grapholita molesta* or the plum fruit moth *Grapholita funebrana.* The mode of action of CpGV is a bi-phasic infection process of the larval stages of the above cited hosts. After oral ingestion of viral occlusion bodies, the virus replicates in the midgut cells (primary infection) and then infection is spread via non-occluded viruses to other body tissues (secondary infection) leading to the insect's death. CpGV is not supposed to have any harmful effects on organisms not belonging to the family of Tortricidae. With regard to environmental safety it is important to note that CpGV and the whole group of baculoviruses are naturally present in the environment. The experience that baculoviruses present no risk to mammals and men has been confirmed by numerous studies. The family of baculoviruses is regarded to be safe for humans and vertebrates confirmed by the inclusion of this virus family in the list of "Qualified Presumption of Safety" published by EFSA[2]. Therefore, their application in pest control means only a fluctuation of the virus titre in the biotope of the pest insect. CpGV and the whole family of baculoviruses are not related to any animal or plant pathogen and it does not produce any metabolite. For these reasons, no harmful effects from CpGV on humans, other vertebrates, other non-target organisms or the environment are expected. According to Commission Regulation (EU) 2016/439[3] *Cydia pomonella* Granulovirus is included into Annex IV of Regulation (EC) No 396/2005[4]. This means that no residue definition applies to the microorganism and no MRL is set for any of the existing or intended uses.

According to the GAP tables for the individual formulated products (see LoEP), *Cydia pomonella* granulovirus is used in pome fruit (apple, pear, quince, nashi, *Mespilus*), stone fruit (peach, apricot, nectarine,

[1] OJL 330, 09.12.2007, p.6
[2] EFSA Journal 2015; 13(12):4331
[3] OJL 78, 23.03.2016, p. 31-33
[4] OJL 70, 23.02.2005, p.1-16

almond, plum) and walnut against the codling moth (*Cydia pomonella*) and the oriental Fruit moth (*Grapholita molesta*).

In the following, for ease of information, full study summaries and sections taken from the original DAR are included if they are considered relevant for renewal of CpGV. In order to facilitate discrimination between new data and data already evaluated during the first approval process, the headline "New information 2016" begins the section with data, which has previously not been submitted or evaluated. Data and their evaluations from the original DAR and addenda to the DAR are highlighted grey.

Specific studies on the ecotoxicity of the active substance *Cydia pomonella* Granulovirus (CpGV) have not been submitted by the notiferes (CpGV Taskforce). Ecotoxicological studies performed with formulated *Cydia pomonella* were submitted. Regarding the active substance, the CpGV Taskforce describe the ecotoxicological properties of baculoviruses on the basis of scientific literature. The biology of granuloviruses is very similar and differs mainly in their isolation. Furthermore, it has to be kept in mind that CpGV is highly specific and has an effect on very few species of the Tortricidae family (Lepidoptera). *Cydia pomonella* Granulovirus CpGV is isolated from codling moth larvae.

Taxonomic name and strain

Please refer to Volume 3MA Section B.1.

Natural occurrence and geographical distribution

Actually all baculoviruses are naturally present in our environment. Their application in pest control means only a fluctuation of the virus titre in the biotope of the pest insect. For further details, please refer to Volume 3MA Section B.2.

Mode of action

The mode of action of CpGV is a bi-phasic infection process of the larval stages of *C. pomonella* and *G. molesta*. After oral ingestion of viral occlusion bodies, the virus replicates in the mid-gut cells (primary infection) and then infection is spread via non-occluded viruses to other body tissues (secondary infection) leading to the insect's death. The body of the insect liquefies and the virus is released into the environment where it can infect other codling moth larvae. The incubation period is independent of the dose of virus consumed by the insect. The various larval stages of the codling moth show different susceptibility: first-instar larvae are more sensitive to infection, and the tolerance increases with age until reaching its maximum at the fourth stage. Some of the larvae with late infection continue to grow but, after having reached the fifth stage, do not manage to form pupae.

Host specificity range and effects on other species than the target harmful organism(s)

Baculoviruses have been found only in arthropods. No member of this family is known to infect vertebrates or plants.

In contrast to NPV, the host range of GV appears to be even more narrow and mostly restricted to a single species (OECD 2002). Reports of successful and unsuccessful attempts to cross-transmit several GV's to alternative hosts are summarised in the following table (for further details, see GRÖNER, 1986; Data point: KMA 8.1, BVL no 3683563):

Table B.9.1-1: CpGV isolated from *Cydia pomonella* and attempted to cross-transmit to alternative lepidopteran hosts

Family	Species	Result
Tortricidae	*Archips podanus*	-

	Archips sorbianus	-
	Adoxophyes orana	-
	Choristoneura muriana	-
	Enarmonia formosana	-
	Grapholita funebrana	-
	Grapholita molesta	+
	Hedya nubiferana	-
	Laspeyresia nigricana	+
	Pandemis heparana	-
	Rhyacionia buoliana	+
	Zeiraphera diniana	-
Geometridae	*Operophtera brumata*	-
Noctuidae	*Agrotis segetum*	-
	Autographa gamma	-
	Heliothis zea	-
	Mamestra brassicae	-
Plutellidae	*Plutella xylostella*	-
Pyralidae	*Amyelois transitella*	-
Saturniidae	*Antheraea pernyi*	-

successful attempts of cross-transmission (+) are in bold, (-) unsuccessful attempt of cross-transmission

This shows that CpGV is very restricted in its infectivity to codling moth (*Cydia pomonella* (L.), Lepidoptera: Tortricidae) only. The high degree of host-specificity is especially important for assessing the side-effects on beneficial arthropods and other non-target organisms.

Representative uses and formulation
Representative uses chosen for renewal of CpGV cover control of Codling moth (*Cydia pomonella*) and Oriental fruit moth (*Grapholita molesta*) in Pome fruit (apple, pear, quince, nashi, Mespilus), Stone fruit (peach, apricot) as well as Walnut. Both, use by professionals and non-professionals is intended. The overall max. total rate per crop/season is 10×10^{13} GV/ha, taking into account 10 subsequent applications at an interval of 10 days.

It is considered that the Critical GAP of CARPOVIRUSINE chosen for the renewal of the active substance CpGV covers worst case exposure scenarios for non-target organisms and the environment.

Critical GAP of CARPOVIRUSINE for renewal of CpGV

Crop and/ or situation	**F G or I**	**Pests or Group of pests controlled**	**Application**			**Application rate per treatment**		
			Method / Kind	**Timing / Growth stage of crop & season**	**Max. number (min. interval between applications) a) per use b) per crop/ season**	**L product / ha a) max. rate per appl. b) max. total rate per crop/season**	**GV / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min / max**
Pome fruit Stone fruit Walnut	F	Codling moth (*Cydia pomonella*) Oriental fruit moth (*Grapholita molesta*)	Foliar spray (tractor drawn)	BBCH 71-89	a) 3-10 (10) b) 3-10 (10)	a) 1 * b) 10	a) 1×10^{13} GV/ha b) 10×10^{13} GV/ha	1000
Pome fruit Stone fruit Walnut	HG **		Foliar spray (Knapsack sprayer)					

*This application rate of 1 L/ha corresponds to 0.1 L/hL in 1000 L water/ha or 0.7 L/ha LWA (leaf wall area)
** HG: Home garden use

Critical GAP of MADEX for renewal of CpGV

Crop and/ or situation	**F G or I**	**Pests or Group of pests controlled**	**Application**			**Application rate per treatment**		
			Method / Kind	**Timing / Growth stage of crop & season**	**Max. number (min. interval between applications) a) per use b) per crop/ season**	**L product / ha a) max. rate per appl. b) max. total rate per crop/season**	**GV / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha/ mch min / max**

Pome fruit Stone fruit Walnut	F	Codling moth (*Cydia pomonella*)	Foliar spray (tractor drawn)	Before first larvae hatch from eggs*	a) 10 (6-8**) b) 10 (6-8**)	a) 0.3×10^{13} GV/ha b) 3×10^{13} GV/ha	a) 0.1 b) 1	400 / 1200
Pome fruit Stone fruit Walnut	HG ***		Foliar spray (Knapsack sprayer)					

mch = m crown height
*First treatment 85 day degrees after the first warm evening with flight activity. Zero point of development of the codling moth is 10°C.
** 6-8 sunny days, counting 2 partially sunny days as 1 day
*** HG: Home garden use

Critical GAP of MADEX TWIN for renewal of CpGV

Crop and/ or situation	**F G or I**	**Pests or Group of pests controlled**	**Application**			**Application rate per treatment**		
			Method / Kind	**Timing / Growth stage of crop & season**	**Max. number / min. interval between applications**	**L product / ha a) max. rate per appl. b) max. total rate per crop/season**	**GV / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min / max**
Stone fruit	F	Oriental fruit moth (*Grapholita molesta*)	Foliar spray (tractor mounted sprayer)	Before first larvae hatch from eggs*	12 / 6 days*	a) 0.3×10^{13} GV/ha b) 3.6×10^{13} GV/ha	a) 0.1 b) 1.2	800
Stone fruit	HG **		Foliar spray (Knapsack sprayer)					

* 6 - 8 sunny days, counting 2 partially sunny days as 1 day
** HG: Home garden use

Critical GAP of VIRGO for renewal of CpGV

Crop and/ or situation	**F G or I**	**Pests or Group of pests controlled**	**Application**			**Application rate per treatment**		
			Method / Kind	**Timing / Growth stage of crop & season**	**Max. number / min. interval between applications**	**L product / ha a) max. rate per appl. b) max. total rate per crop/season**	**GV / ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha/ mch min / max**
Pome fruits and Walnut	F	Codling moth (*Cydia pomonella*)	Foliar spray (tractor drawn)	BBCH 71 - 87	6/7 days	a) 1.5×10^{13} GV/ha b) 9×10^{13} GV/ha	a) 0.75 b) 4.5	1500 - 1700*

*The lower water volume should be used for lower trees, whereas the highest water amount is recommended for trees with a higher leaf area. In case of expanded leaf area which requires more than 1500 L water/ha, a higher water volume can be applied, but the maximum rate of 15×10^{12} GV/ha must be respected.

The aforementioned formulations contain between 1.0 x 10^{13} GV/L and 3.0 x 10^{13} GV/L CpGV, respectively.

New information 2016
A literature search according to EFSA guidance (2011)[5] was conducted in May 2016 covering the last 10 years. The literature research was conducted on the Scopus database (for further details, please refer to chapter B.9.8). Five separate literature searches were conducted using different search terms. A first search focused on the term *Cydia pomonella* Granulovirus and its synonyms. A second search focussed on baculoviruses in general but excluded search terms related to the use of these viruses for the production of recombinant proteins. In addition, some terms (Net present value, Predictive value and related terms) were excluded to limit background noise generated by the search term "NPV", abbreviation of "nucleopolyhedrovirus". Last, three searches were conducted on baculoviruses in general but focussing on specific search terms related to toxicology, ecotoxicology and fate and behaviour in the environment. The search strategy aimed to find all recent (from 2005 onwards) references that are of relevance regarding possible effects of CpGV on non-target organisms. A first search focused on the term *Cydia pomonella* Granulovirus and its synonyms including names of commercial products. After rapid assessment based on title and abstract; 10 references were submitted to full-text analysis. In total, two references were considered relevant and reliable, and are summarised under the respective data points below.

B.9.1 Effects on birds

The following information is derived from the Draft Assessment Report Volume 3, Annex B-9, point B.9.2.

For baculoviruses the following information regarding effects on birds can be derived from literature:
According to Ignoffo (1975, BVL no 3683296) (reference no. IIM 8.1/02) there were no demonstrable cases of viral toxicity or pathogenicity observed within the last decade in studies specifically designed to include pathology in avian species (chicken, turkey, pheasant, dove, mallard, sparrow and quail).
According to Martignoni (1978, BVL no 3683297) (reference no. IIM 8.1/03) none of the avian species tested (mallard duck, ring-necked pheasants, house sparrows, mule deer) showed symptoms or signs of systemic toxicity-pathogenicity, except for minor temporary weakness in some of the test subjects.
Lautenschlager et al. (1979, BVL no 3683299) (reference no. IIM 8.1/04) studied the response of birds to aerial application of the nucleopolyhedrovirus (NPV) of the gypsy moth. No changes in population of the wild birds that could be attributed to the NPV treatment were detected. No significant differences in organ weights or in necropsy and histopathological conditions of organs and tissues were revealed between NPV-treated and control birds. It was concluded that the aerial application of NPV had no short-term adverse effect on birds, neither directly nor secondary by feeding on NPV-infected gypsy moth larvae or on other NPV-contaminated food sources.
From 1965 to 1970 at least 4 species of birds were exposed to heavy doses of *Heliothis* NPV without any adverse reactions (Burges et al. 1980, BVL no 3683298) (reference no. IIM 8.1/05). No adverse effects were reported when English sparrows were fed 8 × 10^9 polyhedral inclusion bodies/kg.
Lewis & Podgwaite (1981, BVL no 3683300) (reference no. IIM 8.1/06) reported that bobwhite quail and mallard ducks were challenged with 100 times the field dose of gypsy moth NPV. No effect was apparent in either species with regard to toxicity, behaviour, or mortality due to the oral administration of the gypsy moth NPV. NPV was fed to the back-capped chickadee and to the house sparrow as NPV-infected gypsy moth larvae (Podgwaite & Galipeau 1978 cited by Lewis & Podgwaite 1981). Analyses of body weights and histopathological examination of organs from NPV-treated birds indicated that NPV had no apparent short-term effects on these two avian predators of the insects. These studies have shown that gypsy moth NPV has no apparent adverse effects on those birds that may utilise the gypsy moth as a food source, or on those birds that may contact the virus from NPV spray, spray residue, or NPV-infected larvae.
No ill effects were observed in acute oral toxicity tests in two species of bird, chickens and turkeys

[5] Guidance of EFSA: Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009. EFSA Journal 2011;9(2):2092

(Burges 1981, BVL no 3683570) (reference no. IIM 8.1/07). In the course of field trials, bee hives were studied and pre-spray and post-spray counts were made of birds. No ill effects were noted (Burges 1981). There was no evidence of the viral preparation *Neodiprion sertifer* NPV having any harmful effects in acute oral tests on mallard ducks and bobwhite quail (Burges 1981).

After ingesting inclusion bodies of a Nucleopolyhedrovirus by chickens, the faeces of these test animals showed virus activity caused by unaltered inclusion bodies (Gröner & Döller 1982, BVL no 3683303) (reference no. IIM 8.1/08). The treatment of the chicken faeces with chloroform had no deleterious effect on the virus activity in the faeces. Therefore, the polyhedra were presumably not solubilised in the alimentary canal of the chickens. An interpretation of the different behaviour of polyhedra in the alimentary tract of birds could be based on the results of previous studies which indicated that polyhedra were not attacked by trypsin (at pH 9.2) within 18 h unless they were pre-treated with HCl at pH 1 for 2 h (Gröner 1978 cited by Gröner & Döller 1982). The low acidity in the stomach of birds may result in an insufficient pre-treatment of the polyhedra which would leave them resistant to the intestinal alkaline protease.

To test the safety to vertebrates of the granulovirus of *Pieris rapae* in China, the virus was administered at 50 mg/kg body weight as a single oral dose to birds. None showed ill effects and growth was normal during the 2-3 months that followed the administration (Xuebao 1982, BVL no 3683558) (reference no. IIM 8.1/09).

Gröner (1990, BVL no 3683559) (reference no. IIM 8.1/10) reported that no member of the baculovirus family is known to infect vertebrates.

Mortality from naturally occurring nucleopolyhedrovirus (NPV) among gypsy moth, *Lymantria dispar* (L.) larvae was 15 % in three species of birds captured in the wild from 2 plots (Lautenschlager et al. 1980, BVL no 3683560) (reference no. IIM 8.1/11).

Entwistle et al. (1978, BVL no 3683561) (reference no. IIM 8.1/12) studied the passage of a Nucleopolyhedrovirus (NPV) through the gut of birds during cage tests. Following brief infection feeds, polyhedral inclusion bodies of the virus could be detected in bird faces within 0.5 h. Peak passage of polyhedra occurred in less than one hour and none were detected after 2.5 h The feces of all birds remained infective (in bioassay tests using first instar *Gilpinia hercyniae* larvae) to the end of the day of infection while those of nine birds remained infective to the next day and of six birds to the third day. One bird was infective up to day 7. The infectivity of NPV in feces stored for 2 years at +3°C declined by half. The comparatively long retention and passage of infective virus suggests birds may be effective in short- and long-distance transport of baculoviruses. Polyhedral inclusion bodies of baculoviruses pass undegraded through the alimentary tract of all bird species so far tested (summarised in Entwistle et al. 1971 and cited in Entwistle et al. 1978), indicating that an acidic milieu apparently has no effect on polyhedral inclusion bodies (PIBs) or on the virions they contain. The protein matrix of PIBs is dissolved in mildly alkaline conditions and when the polyhedral membrane is destroyed proteolytic digestion of the matrix may occur (Entwistle et al. 1978).

Gröner (1986, BVL no 3683563) (reference no. IIM 8.1/13) reported that birds have the potential for trans-porting NPVs within "contaminated" ecosystems and even for passing faeces containing infective NPVs (*Gilpinia hercyniae* NPVs) throughout the nonlarval winter period as a result of their feeding on the cadavers of NPV-killed larvae adhering to trees. According to the above named authors birds were able to pass polyhedra through their alimentary tracts in amounts great enough to kill larvae of the corresponding test species in bioassays. After aerial application of the gypsy moth NPV, data from 23 caged quails and 53 free-living birds showed no differences for any species between NPV-treated and control birds as judged by organ weights or necropsy and histopathological rankings of the conditions of organs and tissues. An aerial application of the NPV from the red-headed pine-sawfly, *N. lecontei*, did not cause any adverse immediate or short-term impact upon bird populations located in the treated areas. Similarly, no deleterious effects on small forest songbirds were attributed to an aerial application of the spruce budworm NPV. High single-dose levels of technical virus preparations of the *Orgyia pseudotsugata* NPV fed to mallard ducks, ring-necked pheasants, and English sparrows did not produce any symptoms or signs of systemic toxicity nor pathogenicity, except for minor temporary weakness in a few test subjects.

Conclusion:

The above mentioned literature demonstrates that there are no effects to birds caused by baculoviruses and CpGV, respectively.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to birds did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

B.9.2 Effects on aquatic organisms

B.9.2.1 Effects on fish

The following information is derived from the Draft Assessment Report Volume 3, Annex B-9, point B.9.3.1.

For baculoviruses the following information regarding effects on fish can be derived from literature:
Banowetz et al. (1976, BVL no 3683920) (reference no. IIM 8.2/02) showed that the use of baculoviruses as an agent to control *Orgyia pseudotsugata* infestations should have no deleterious effects on chinook salmon, coho salmon or steelhead trout which reside in waters adjacent to treated forests. Coho salmon seems reluctant to eat *O. pseudotsugata* larvae. The virus does not persist in these fish. Fingerlings (average weight 0.5 g) of the three species and smolts (average weight 20 g) of coho salmon were exposed to virus by intraperitoneal injection, by feeding, and in the water. The virus caused no pathological changes. Bioassay of tissue homogenates from kidney, liver, spleen, and digestive tract of coho salmon smolts showed that the virus was cleared or inactivated rapidly (within 24 h after exposure). All attempts to feed tussock moth larvae to coho salmon smolts failed. The fish, even when deprived of food for 5 d, rejected the larvae (including larvae coated with serum albumin), but they did not reject earthworms cut to the size of larvae.
Gröner et al. (1981, BVL no 3683565) (reference number IIM 8.2/03) reported that two baculoviruses of moth caterpillars act strictly lepidopteran-specific does not extend beyond the Lepidoptera. There is surely no doubt that moth caterpillars are not a principle source of food for fish. The authors have found no indications of hazard to at least 12 fish species and at least six fish cell lines by entomopathogenic viruses in the published literature. Moreover high virus titres can also occur naturally during mass reproduction of moth and sawfly larvae. This means that aquatic organisms have always been confronted by considerable numbers of baculoviruses under natural conditions without any observable damage.
Also, Gröner (1986, BVL no 3683912) (reference no. IIM 8.2/04) and Gröner (1990, BVL no 3683806) (reference no. IIM 8.2/05) reported no adverse effects of NPVs on different fish species from the published literature.
Hicks et al. (1981, BVL no 3683926) (reference no. IIM 8.2/06) investigated the effects of a Nucleopolyhedrovirus (NPV) of the red-headed pine sawfly, *Neodiprion lecontei*, on rainbow trout, *Salmo gairdneri*. The fish were exposed to this virus by intubation and topical application and no ill-effects were observed.
Burges et al. (1980, BVL no 3683610) (reference no. IIM 8.2/07) reported that from 1965 to 1970 at least 7 fishes were exposed to heavy doses of *Heliothis* NPV without any adverse reactions.
Bluegill sunfish and rainbow trout were exposed to *N. sertifer* NPV in aquaria (F.B. Lewis, personal communication cited by Burges 1981, BVL no 3683301) (reference no. IIM 8.2/06). There was no evidence of the viral preparation having any harmful effects.
Lewis & Podgwaite (1981, BVL no 3683800) (reference no. IIM 8.2/09) conducted ninety-six hour static exposure tests with 240 juvenile bluegills and 240 juvenile brown trout. As a result of this study, which examined the effects of gypsy moth NPV on survival and histopathology of bluegills and brown trout, it was concluded that the NPV had no demonstrable effect on either species at doses approximately 100 times of the field application dose.
In order to test the safety of the granulovirus of *Artogeia rapae* (L.) (*Pieris rapae*) in China, the virus was administered at 50 mg/kg body weight as a single oral dose to fish (Xuebao 1982, BVL no 3683905) (reference no. IIM 8.2/10). None showed ill effects and growth was normal during the 2-3 months that followed the administration.

Five fish species (killifish, spotfish, white sucker, sheepshead minnow, and rainbow trout) were systematically exposed to the major kinds of NPV insect viruses (Ignoffo 1975, BVL no 3683600) (reference no. IIM 8.2/11). There were no demonstrable cases of viral toxicity of pathogenicity observed within the last decade in studies specifically designed to induce pathology in vertebrates.

The above presented data from the original DAR can be supplemented with the following public literature information (not previously submitted): Immunological effects of baculovirues in fish have been investigated by Ashour et al. (2007, BVL no 3306476). Groups of 10 fish (*Tilapia nilotica*) received a dose of 1 x 10^9 PIBs of either wild type *Spodoptera littoralis* NPV (SlNPV), wild type *Autographa californica* multiple NPV (AcMNPV), or a recombinant (i.e., genetically modified) *Autographa californica* NPV for two days in their standard diet. 30 days later, the anterior part of the kidney ("head kidney", i.e., an organ that is analogous to the bone marrow in mammals and the site of haematopoiesis) was excised and the phagocytic activity of macrophages was determined by means of an assay in which formalin-killed *E. coli* was applied. The fish tolerated the treatment (no mortality in treated and untreated fish 28 days after treatment), but, in all virus-treated groups, phagocytic activity was lower than in the control group after 30 minutes of the assay. However, over the subsequent time period, phagocytic activity increased and, after 180 minutes, there were virtually no differences to the control group left.
Kreutzweiser et al. (1997) investigated the infectivity and effects on rainbow trout (*Oncorhynchus mykiss*) fingerlings of NPVs from two forest insect pests, the gypsy moth, and the eastern spruce budworm. Rainbow trout fingerlings were fed dried krill injected with gypsy moth or spruce budworm nuclear polyhedrosis virus (LdNPV and CfNPV, respectively) at a total dose of 1.4×10^7 occlusion bodies (OBs) per fish. After 21 days of exposure there were no adverse effects on fish survival or behavior and no significant differences in feeding rates or growth between treated and control fish. The internal organs of all fish were examined at the end of the experiment and there were no signs of lesions, discoloration, swelling, hemorrhaging, or other aberrations. Visceral tissues were analyzed with a horseradish peroxidase-labeled whole genomic DNA probe to detect infection by the NPVs. There were no indications of NPV infection in stomach and intestinal tract tissues of treated fish.

Conclusion:
The above mentioned literature demonstrate that there are no effects to fish caused by baculoviruses and CpGV, respectively.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to fish did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

B.9.2.2 Effects on freshwater invertebrates

The following information is derived from the Draft Assessment Report Volume 3, Annex B-9, point B.9.3.2.

For baculoviruses the following information regarding effects on freshwater invertebrates can be derived from the literature:
The LC_{50} value (48 h) of CpGV for *Daphnia pulex* de Geer was found to be > 250 mg/L (Copping, 2001, BVL no 3683588) (reference no. IIM 8.3/01).
Gröner (1986, BVL no 3683913) (reference no. IIM 8.3/02) and Gröner (1990, BVL no 3683807) (reference no. IIM 8.3/03) reported that the application of *Heliothis zea* NPV to *Daphnia* resulted in no adverse effects.
In the study conducted by Hicks et al. (1981, BVL no 3683926) (reference no. IIM 8.3/04) no ill-effects were detected in *Daphnia pulex* when the Nucleopolyhedrovirus (NPV) of the red-headed pine sawfly, *Neodiprion lecontei* was added to their culture. No significant differences ($p < 0.05$) were noted in brood size or fecundity in individual daphnia between treated and control groups. A total of 60 daphnia was assessed histologically and no lesions or abnormalities were noted in any of the tissues examined. The alimentary canals frequently contained ingested suggestive of algae and fragmented material resembling

that found in the uninfected and NPV-infected larval preparation.
Burges et al. (1980, BVL no 3683611) (reference no. IIM 8.3/05) found that water fleas were not susceptible to 10^6 to 10^9 PIB (polyhedral inclusion bodies) animal.
Lewis & Podgwaite (1981, BVL no 3683801) (reference no. IIM 8.3/06) also reported that survival of *Daphnia* was unaffected by exposure to the NPV during their development from first instar to adult. Further, the development time of the immatures and subsequent reproduction of the treated adults was comparable to control insects.

Conclusion:
The above mentioned literature demonstrates that there are no effects to aquatic crustaceans caused by baculoviruses and CpGV, respectively.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to aquatic invertebrates did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

B.9.2.3 Effects on algae growth

No data on effects of the active substance on algal growth were submitted for first valuation of the CpGV. Furthermore, no new data has been submitted for the AIR4 procedure. Instead, studies on the formulated products VIRGO, Granulovirus CpGV SC and CARPOVIRUSINE were submitted for first evaluation. For detailed study summaries, please refer to the Draft Assessment Report Volume 3, Annex B-9, point B.9.3.3.2 and the original dossier Annex IIIM point 10.2.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to algae did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

B.9.2.4 Effects on plants other than algae

No data on effects of the active substance on plants other than algae were submitted for first valuation of the CpGV. Furthermore, no new data has been submitted for the AIR4 procedure. Instead studies on the formulated products VIRGO and Granupom were submitted for first evaluation. Please refer to the Draft Assessment Report Volume 3, Annex B-9, point B.9.3.4.2 and the original dossier Annex IIIM point 10.2.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to plants other than algae did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

The following information in the paragraph below is derived from the Draft Assessment Report Volume 3, Annex B-9 and gives an overview of the data on aquatic organisms (toxicity, infectiveness and pathogenicity) for the available studies with the formulated products.

No special studies referring the active substance *Cydia pomonella* GV were supplied by the notifier. The submitted literature describing effects of baculoviruses on fish and aquatic invertebrates does not allude to any toxic, infective or pathogenic effects. CpGV is also not expected to have any adverse effect on algae.
Aquatic toxicity tests were conducted with the formulated products Granupom (CpGV SC), CARPOVIRUSINE and VIRGO containing 2.2×10^{13}, 1×10^{13} and 2×10^{13} granules CpGV/L, respectively. The tests on acute effects on fish and aquatic invertebrates and on long-term effects on algal growth and aquatic plants led to the endpoints summarised in table below. The effect concentrations given in µg product/L were converted to number of granules CpGV/L using data from the "Summary of Good Agricultural Practice":

Test substance	Conc. of active substance in product (granules/L)	Conc. of active substance in product (granules CpGV/kg)
CPGV SC	2.2×10^{13}	1.90×10^{13}
VIRGO	2×10^{13}	1.61×10^{13}
CARPOVIRUSINE	1×10^{13}	0.83×10^{13}
Granupom	3.4×10^{10}	$2{,}93 \times 10^{10}$

* density of Granupom 1.16 g/mL, VIRGO 1.24 g/mL, CARPOVIRUSINE no data, 1.2 g/mL assumed (see B.1)

B.9.2.5 Summary of the studies on aquatic organisms toxicity, infectiveness and pathogenicity

Summary of the studies on effects on aquatic organisms (adapted from the DAR, 2007)

Group	Test substance	Species	Duration and realisation of test[3]	Endpoint (L/EC_{50})	Toxicity [mg product/L] designation nom./real	Toxicity [granules CpGV /L]
Toxicity						
Fish – acut	CpGV SC VIRGO CARPOVIRUSINE	*Oncorhynchus mykiss* *Danio rerio*	4 d; static 4 d; static	LC_{50} LC_{50}	> 100 nom[1]. > 100 nom [2] > 250 nom.	$> 1.90 \times 10^9$ $> 1.61 \times 10^9$ $> 2.08 \times 10^9$
Invertebrates – acut	CpGV SC VIRGO CARPOVIRUSINE	*Daphnia magna*	2 d; static	EC_{50}	> 100 nom[2]. > 100 nom[2] > 250 nom[2]	$> 1.90 \times 10^9$ $> 1.61 \times 10^9$ $> 2.08 \times 10^9$
Algae	CpGV SC VIRGO CARPOVIRUSINE	*D. subspicatus* *P. subcapitata* *P. subcapitata*	3 d; static	EC_{50}	> 100 nom[2]. > 100 nom[2]. > 100 nom[2].	$> 1.90 \times 10^9$ $> 1.61 \times 10^9$ $> 0.83 \times 10^9$
Aquatic plants	Granupom VIRGO	*Lemna gibba*	7 d; static	EC_{50}	> 100 nom[2] > 100 nom[2]	$> 2.39 \times 10^6$ $> 1.61 \times 10^9$
Infectiveness	no information, endpoints not included in the study design					
Pathogenicity	endpoints not included in the study design					

[1] all fish exposed to 100 mg Granupom/L showed a change in pigmentation to a dark colour
[2] no effects at this concentration, no observations
[3] static, semi = semi-static, flow = flow through

Comment RMS:

Eventhough the experimental study findings on aquatic organisms presented above lack information on infectiveness and pathogenicity endpoints, detrimental impacts on the non-target species are not expected due to the very narrow host range of CpGV (restricted to a few species within the Family Tortricidae). Additional information is not deemed necessary.

B.9.3 Effects on Bees

Cydia pomonella Granulovirus (CpGV), natural entomopathogen, belongs to the family Baculoviridae acts as insecticide for the biological control of the codling moth, *Cydia pomonella* and will be used in orchards. CpGV is naturally present in the environment. The isolates used for the submitted representative formulations were all derived from the Mexican isolate originally isolated in 1963 and are not genetically modified.

No new GLP studies on the toxicity, infectiveness, or pathogenicity of the active substance (CpGV) to honey bees, bumble bees and solitary bees have been submitted since the first EU evaluation. However, one new laboratory study on bumble bees has been generated by a literature research and will be reported in detail in this chapter (B.9.3.1/1 (Mommaerts et al, 2009, BVL no 3306491)). Information on data already evaluated are not further reported, but will be presented as briefly summaries below (refer to Table 9.3-1, Table 9.3-2).
The inclusion of results obtained with other baculoviruses in this dossier is justifiable due to the close similarity of all baculoviruses.

Table B.9.3-1: Ecotoxicological studies according to EPPO 170

<table>
<tr><th>Test item</th><th>Test species
Study design
Guideline
GLP status</th><th>Endpoint</th><th>Findings</th><th>Status of evalua-tion</th><th>Reference (Report No.)
Annex point</th></tr>
<tr><td rowspan="2">Carpovirusine</td><td rowspan="2">Apis mellifera (individual)
Laboratory acute toxicity
OECD 213/214
GLP</td><td>LD_{50}
oral 48 h</td><td>> 108.4µg prod-uct/bee**
(> 1.63 x 10^6 CpGV/bee)</td><td rowspan="2">Already evaluated</td><td>Schmitzer, S. (2006)
26194035
BVL no 3689722</td></tr>
<tr><td>LD_{50}
contact 48 h</td><td>> 100µg prod-uct/bee**
(> 1.63 x 10^6 CpGV/bee)</td><td>MP B 9.3.1/1</td></tr>
<tr><td rowspan="2">Virgo</td><td>Apis mellifera (individual)
Laboratory acute toxicity
OECD 213/214, EPPO 170
Non-GLP</td><td>LD_{50}
oral 72 h</td><td>> 100 µg prod-uct/bee**
(> 1.63 x 10^6 CpGV/bee)</td><td rowspan="2">Already evaluated</td><td>Colli, M. (2005)
Rep. No.: BT008/05
BVL no 1300695</td></tr>
<tr><td>Apis mellifera (individual)
Laboratory acute toxicity
OECD 213/214, EPPO 170
Non-GLP</td><td>LD_{50}
contact 72 h</td><td>> 100 µg prod-uct/bee**
(> 1.63 x 10^6 CpGV/bee)</td><td>MP B 9.3.1/1</td></tr>
<tr><td rowspan="2">Madex*</td><td>Apis mellifera (individual)
Laboratory acute toxicity
EPPO 170
GLP</td><td>LD_{50}
oral 48 h</td><td>> 3.5 x 10^7 CpGV/bee**</td><td rowspan="2">Already evaluated</td><td>Kling, A. (2002)
20011323/01-BLEU
BVL no 1914013</td></tr>
<tr><td>Apis mellifera (individual)
Laboratory acute toxicity
EPPO 170
GLP</td><td>LD_{50}
contact 48 h</td><td>> 4.4 x 10^7 CpGV/bee**</td><td>MP B 9.3.1/1</td></tr>
</table>

CpGV: *Cydia pomonella* Granulovirus
* tested as Granupom (also for approval of Madex Twin a comparable formulation of MADEX). The two formulations Granupom (2.2 x 10^{13} granules/L) and Madex/Madex Twin (3 x 10^{13} granules/L) contains nearly the same amount of granules/L. Therefore, their comparability is considered as sufficient
** EU agreed endpoint; EFSA Journal 2012; 10 (4):2655

Table B.9.3-2: Literature research

Test item	Test species Study design Guideline GLP status	Endpoint	Findings	Status of evaluation	Reference (Report No./BVL-Reg.-No.)
CpGV *	*Bombus terrestris* (colony) Laboratory study No guideline Non-GLP	Mortality, behaviour	No effects	New literature	Mommaerts, V. et al., (2009) M-530333-01-1 BVL no 3306491
CpGV	*Apis mellifera* (individual) Review article No guideline Non-GLP	LD_{50} contact	> 1 x 10^{10} CpGV ml/bee	Already evalu-ated**	Copping, L. G., (2001) BIE2006-65 BVL no 1300650
Studies on the infectiveness to bees					
Baculovirus	*Apis mellifera* (colony) Review article No guideline Non-GLP	No abnormalities in egg production, brood rearing, worker and queen mortality, general colony behaviour		Already evalu-ated**	Gröner, A., (1990) BIE2006-121 BVL no 1300651
Studies on the pathogenicity to bees					
CpGV	*Apis mellifera* (individual) Laboratory study According to BBA guideline VI, 23-1 Non-GLP	Feeding, wetting, contact and vapour exposure	No acute or pathogenic effects	Already evalu-ated**	Gröner, A., (1978) BIE2003-65 BVL no 2019293
Carpocapsa pomonella Granulovirus (synonym for CpGV)	*Apis mellifera* (colony) Laboratory study Guideline/GLP status: No information available	No effects on colony development. ***		Already evalu-ated**	Knox, (1970) BIE2006-123 BVL no 3689576
Argyrotaenia velutinana Granulovirus	*Apis mellifera* (colony) Field study No guideline Non-GLP	No effects on colony development.		Already evalu-ated**	Cantwell et al., (1966)

CpGV: *Cydia pomonella* Granulovirus
* tested as Granupom
** initial evaluation for Annex I inclusion (2007) and the final DAR addendum (2012)

*** Details regarding test methods (e.g. number of controls, replicates, exposure period, bee colony size) are not reported in this short publication. Thus, the present article alone is not considered sufficient. Missing information can be obtained from the previously published bee colony study by Cantwell et al. (1966) and therefore reference should be made to this particular study. However, it should be noted that the study duration slightly differed from the study by Cantwell et al. (1966), namely 4 months instead of 3 months.

B.9.3.1 Toxicity to Bees

Report:	B 9.3.1.1/1 Mommaerts V. et al. (2009): A laboratory evaluation to determine the compatibility of microbiological control agents with the pollinator *Bombus terrestris* Pest Management Science Vol. 65 (9) pp. 949-955; M-530333-01-1, 2970353/445374, BVl no 3306491
Guidelines:	No, study generated by a literature research
GLP:	No
Conclusion RMS:	**The results were considered as supportive information for the risk assessment.** RMS principally agrees with the conclusion of the study, so that the results were considered as supportive information for the risk assessment. However, the exposure duration in the oral tests of 11 weeks and an application volume of 50 µL per bumble bee is regarded as unrealistic, since it is very unlikely that one bumble bee would be exposed to 50 µL of spray solution under practical conditions when *Cydia pomonella* Granulovirus will be used as proposed. Findings indicate no adversely effects on the test organisms.

Executive summary

This study was undertaken to identify any potential adverse side effects of the use of seven mi-crobiological control agents (MCAs) on the bumble bee, Bombus terrestris L., in the context of combined use in integrated pest management (IPM).AQ10 (Ampelomyces quisqualis), Binab-T-vector (Hypocrea parapilulifera+T.atroviride;1/1), Prestop-Mix (Gliocladium catenulatum J1446), Serenade WP (Bacillus subtilis QST713), Trianum-P (Trichoderma harzianum T22), BotaniGard (B. bassiana GHA) and Granupom (Cydia pomonella granulovirus), comprising five biofungicides and two bioinsecticides, were investigated. Bumble bee workers were ex-posed under laboratory conditions to each MCA at its maximum field recommended concentra-tion (MFRC) via three different routes of exposure: dermal contact and orally via either treated sugar water or pollen. Here only data on the product Granupom (active substance: *Cydia pomonella* Granulovirus, concentration 2.2×10^{13} CFU/g) are referred.

MATERIALS AND METHODS

Test design:	Laboratory study considering three different routes of exposure: dermal contact and orally via treated sugar water or pollen
Test item:	Granupom SC (2.2×10^{13} CFU/g) of *Cydia pomonella* Granulovirus
Test organism:	Bumble bees colonies (*Bombus terrestris* L.)

Experimental design

Replicates:	Four microhive colonies consisting of five workers in artificial plastic nest boxes (15x15x10 cm) for each treatment (total of 20 bumble bees per treatment)
Treatments:	Test Item: 4 different concentrations of Granupom SC Toxic reference: Confidor (imidacloprid, 200g/L)
Control:	Tap water, untreated sugar water, water-treated pollen
Application rate:	The maximum field recommended concentration (MFRC) of Granupom SC at 6.6×10^{12} CFU/L and dilutions of 1/2, 1/5 and 1/10 applied via three different exposure routes: contact by topi-cal appli-cation, oral by either treated sugar water or treated pollen.

The MFRC of Granupom SC after dilution with water (1.5 % w/v) was 76.6 × 1012 CFU/L. In addition, effects of a series of dilutions of the MFRC (1/2, 1/5, 1/10) were investigated. All experiments were performed with worker bumble bees obtained from a continuous mass rearing programme and conducted under standardised laboratory conditions of 28–30°C, a relative humidity (RH) of 60-65 % and continuous darkness. The insects were provided ad libitum with commercial sugar water.
Four artificial nests, each containing 5 newly emerged workers, were exposed for each treatment (contact, oral via sugar, oral via pollen). Each experiment was repeated twice. For each treatment, worker mortality was scored after 72 h and on a weekly basis during a period of 11 weeks. For the contact treatments, the MFRC was prepared in water. Individual bees were topically treated with 50 µL of this aqueous solution on their dorsal thorax with a micropipette. For the oral treatments, bumble bee workers were continuously exposed to 500 mL of sugar water that was dosed with Granupom SC or to pollen sprayed until saturation with Serenade WP in water. The treated sugar water and pollen were replaced weekly with freshly prepared material. In addition, as positive controls, workers were also treated with a neonicotinoid insecticide formulation, imidacloprid 200 g/L SL at its MFRC (200 mg a.s./L) via the three exposure methods.

Observations:	Mortality was assessed daily for the first three days and on a weekly basis during a period of 11 weeks.

RESULTS AND DISCUSSION

Granupom SC did not exhibit any lethal effects against bumble bee workers during the first 72 h following contact or oral treatment. After 11 weeks, the exposure to Granupom SC via contact and orally to treated sugar solution resulted, at concentrations up to the MFRC, also in none lethal effects. An oral exposure of worker bumble bees to treated pollen at the MFRC of Granupom SC did not lead to an increased mortality after 11 weeks.

Furthermore, nests exposed by contact to Granupom SC at its MFRC resulted in reproductive rates and production of drones that were not significantly different ($P > 0.05$) from those observed in the control after 11 weeks.

CONCLUSIONS by the applicant

Cydia pomonella Granulovirus applied as Granupom SC at maximum field realistic application rates of 6.6×10^{12} CFU/L is low toxic via oral or contact exposure to bumble bees *(Bombus terrestris* L.) with no adversely effects.

B.9.3.2 Infectiveness to Bees

No new tests regarding the infectiveness of *Cydia pomonella* Granulovirus (CpGV) were submitted. The information from the literature review, listed several studies, in which the impact on honey bee colonies were tested, and the results do not indicate any harmful effects on brood and colony development (Cantwell et al., 1966; Knox, 1970, BVL no 3689576; Gröner, A., 1978, BVL no 2019293; Gröner, A., 1990, BVL no 1300651). In addition, no signs of an impact of brood development in bumble bees colonies could be detected in another study (Mommaerts, V. et al., 2009, BVl no 3306491). Accordingly, together with the high host specificity of CpGV to only a few species of Tortricidae family (Lepidoperta), the risk for bee larvae or, in general, for the bee brood could be assumed as negligible. No further data is required. Information on data already evaluated in the initial evaluation of CpGV (2012) are not further reported, but will be presented as briefly summaries (refer to Table B.9.3.1-2).
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B.9.3.3 Pathogenicity to Bees

No new tests regarding the pathogenicity of *Cydia pomonella* Granulovirus (CpGV) were submitted. The information from the literature review, listed several studies, in which the impact on honey bee colonies were tested, and the results do not indicate any harmful effects on brood and colony development (Cantwell et al., 1966; Knox, 1970, BVL no 3689576; Gröner, A., 1978, BVL no 2019293; Gröner, A., 1990, BVL no 1300651). In addition, no signs of an impact of brood development in bumble bees colonies could be detected in another study (Mommaerts, V. et al., 2009, BVl no 3306491). Accordingly, together with the high host specificity of CpGV to only a few species of Tortricidae family (Lepidoperta), the risk for bee larvae or, in general, for the bee brood could be assumed as negligible. No further data is required. Information on data already evaluated in the initial evaluation of CpGV (2012) are not further reported, but will be presented as briefly summaries (refer to Table B.9.3.1-2).

B.9.4 Effects on arthropods other than bees

The following information is derived from the Draft Assessment Report Volume 3, Annex B-9, point B.9.6.

The family *Baculoviridae* comprises two genera: the nucleopolyhedroviruses (NPV) and the granuloviruses (GV). *Cydia pomonella* Granulovirus belongs to the family Baculovirus and the genus Granulovirus. Baculoviruses are naturally present in our environment. The application of them as a microbial pest control agent means only a fluctuation of the natural virus titre.

For baculoviruses the following information regarding effects on other arthropod species can be derived from the literature:

CpGV is considered to be harmless to the predatory mites *Typhlodromus pyri* Scheuten and *Amblyseius californicus* (McGregor) (Copping, 2001, BVL no 3683590) (reference no: IIM 8.8/01).

Ignoffo (1975, BVL no 3683601) (reference no. IIM 8.8/02) reported that within the insect, there are reports of virus cross-transmission between species of the same genus, fewer between species of the same family, less between families of the same order and still less between orders. However, examples of virus cross-transmission across all taxa including orders are reported for every group of insect virus except of granuloviruses. There are also several reports of a very limited host spectrum for NPV. A specific isolate of NPV of *Heliothis zea*, could be transmitted to four other species of the same genus but not to other lepidopterans, dipterans, hymenopterans, homopterans, and mites. The virus was mostly fed to these species at doses 10 to 100 times the field dose. NPV and GV have similar levels of specificity. The granuloviruses appear to be the most specific of all insect viruses. On 6 of 52 (approx. 12%) attempts at cross-transmitting GV were successful.

Some NPVs may be specific to one host species, e.g. the NPVs of some sawflies (Burges et al. 1980, BVL no 3683612). The NPV of *Heliothis* attacks only 7 moth species, all in the genus *Heliothis* (Ignoffo 1968; Harpaz & Zlotkin 1965; Teakle 1973; Patel et al. 1968 cited by Burges et al. 1980, reference no.

IIM 8.8/03). The NPV of *A. californica* has a wider host range, 13 moth species, spanning several different genera and families of lepidoptera. The NPV of *Heliothis* could not be transmitted to 22 other lepidopterans nor to 15 species in non-lepidopteran insect orders, fed or topically treated at 10 - 100 times the recommended field rate, also not to *Galleria mellonella* (L.), *Nomophila noctuella*, *Trichoplusia ni*, *Musca domestica* injected with virions (Ignoffo 1968; 1973 cited by Burges et al. 1980). Ignoffo 1968 cited by Burges et al. 1980 listed only 3 out of 9 successful attempts to transmit NPVs across insect orders and 30 out of 137 across families.

According to Huber (1978, BVL no 3683575) (reference no. IIM 8.8/04) granuloviruses (GV) seem to be more specific than nucleopolyhedroviruses (NPV). There are not only less reports of successful transmission from the original host to another with GVs, but also their occurrence is limited to the order of Lepidoptera (Huber 1978). NPVs have been reported already in 7 different orders of insects (Huber 1978). Huber (1978) suggests that in case of an apparent successful transmission from one species to another, it is possible that the alien virus only induced a virosis already present in the new host in a latent form (Huber 1978). A preliminary field trial with the codling moth GV to control *R. buoliana* has given encouraging results. Codling moth and European pine shoot moth were found to be susceptible also to the NPV of *Choristoneura murinana*. Though the virulence of this virus is much lower than that of the GV and it is therefore unsuited for control of codling moth, it is useful for the biochemical and serological characterisation studies to have another baculovirus from the same host for comparison. Concluding, the CpGV seems to be infective only to some species within the same subfamily, whereas for the NPV of *C. murinana* susceptible hosts were found in both subfamilies of the Tortricidae. Beside the tortricids listed in Table B. 9.6 1, the following other Lepidoptera were tested for their susceptibility to the CpGV, all with negative results: *Operophtera brumata*, *Autographa gamma*, *Agrotis segetum*, *Mamestra brassicae*, *Heliothis zea*, *Amyelois transitella*, *Plutella maculipennis*, *Antheraea pernyi*.

Table B.9.4-1: Results of attempts to cross transmit the granulovirus of of *Cydia pomonella* (CpGV) [formerly known as *Laspeyresia pomonella* (LpGV)] and the nucleopolyhedrosis virus of *Choristoneura murinana* (CmNPV) to other tortricid species by free ingestion

Fam. Tortricidae Subfamily	Tribe	Species	LpGV [a)] (=CpGV)	CmNPV [a)]	Natural infection [b)]
Tortricinae	Archipini	*Archips podanus*	-		
		Archips sorbianus	-		
		Archips argyrospila	+		
		Pandemis heparana	-		
		Adoxophyes reticulana	-	-	GV, NPV
		Choristoneura murinana	-	+	GV, NPV
		Choristoneura rosaceana	+		
Olethreutinae	Laspeyresiini	*Cydia pomonella*	+	+	GV
		Cydia nigricana	+		
		Grapholitha molesta	+	-	
		Grapholitha funebrana	-	+	
		Enarmonia formosana	-	-	
	Eucosmini	*Rhyacionia buoliana*	+	+	
		Rhyacionia frustrana	+		
		Zeiraphera diniana	-		GV
	Grapholitini	*Cryptophlebia leucotreta*	+		
	Olethreutini	*Hedya nubiferana*	-	-	

a) +: successful; -: unsuccessful; missing: not tested
b) literature records of natural infections with baculoviruses of the corresponding species (Martignoni and Iwai, 1977 (cited by Huber 1978): USDA For. Serv. Gen. Techn. rep. PNW – 40)

The studies above show that the CpGV is highly specific. Only lepidoptera of the familiy Torticidae are infected. So far, only two insect species belonging to the Tortricinae and five insect species, belonging to the Olethreutinae, have been found to be susceptible to it. They also demonstrate the potential of cross transmission experiments for finding new pathogens of important pest insects as e.g. in the case of *Rhyacionia buoliana*.

Jaques et al. (1981, BVL no 3683576) (reference no. IIM 8.8/05) found that treatment of apple trees with LpGV (CpGV) substantially reduced deep-entry damage by *C. pomonella* larvae compared to non-treated check trees in most of the tests in this series. LpGV (CpGV) had little effect on populations on insects predaceous on *L. pomonella* (*C. pomonella*) (thrips, clerids, pentatomids and mirids). The lack of effect of CpGV (LpGV) on species of insects that prey on eggs and larvae of *L. pomonella* (*C. pomonella*) and on the red mite indicated the value of the virus in an integrated pest management system.

In long-term field trials set up to study the influence of the codling moth granulovirus (CpGV) on the apple fauna, the parasitisation of the codling moth and of apple leafrollers were also kept under observation on experimental fields (Dickler 1986, BVL no 3683578) (reference no. IIM 8.8/06). By means of decimating the host population, the CpGV-treatments were seen to have a notable effect on the population of the codling moth parasites.

In cross-infectivity tests conducted by Huber (1995, BVL no 3683579) (reference no. IIM 8.8/07), the granulovirus of the codling moth, *Cydia* (*Laspeyresia*) *pomonella* was found to infect also larvae of the European pine shoot moth, *Rhyacionia buoliana*. In a bioassay with neonate larvae of the European pine shoot moth, placed individually on pine shoots which had been dipped into suspensions of the granulovirus, the LC_{50} was about 10^4 virus capsules/mL. In a small field trial on pine trees enclosed in Saran cages, application of a virus suspension containing 10^8 capsules/mL reduced the European pine shoot moth infestation by 90%.

Lewis & Podgwaite (1981, BVL no 3683803) (reference no. IIM 8.8/08) reported that longevity of *Apanteles melanoscelus* females, percent parasitisation, and sex ratio of emerging next-generation wasps was not significantly different between treatment with *L. dispar* NPV and control. Ten Lepidopterous, two Hymenopterous, one Coleopterous, one Orthopterous, and one Dipterous species were challenged with L. dispar NPV at a dose of 1.5×10^8 PIB's per mL (Lewis & Podgwaite 1981). Despite the high doses, no apparent effect of these treatments was noted.

According to Xuebao (1982, BVL no 3683906) (reference no. IIM 8.8/09) the granulovirus of *Artogeia rapae* showed no ill effects on silkworms (*Bombyx* spp.) and growth was normal during the 2-3 months that followed the administration.

No deleterious effects on beneficial insects resulting from NPV treatment were found (Gröner 1986, BVL no 3683915) (reference no. IIM 8.8/10). However, there may have been some indirect effects on certain entomophagous insects resulting from the death of the host insect from a virosis before the development of the parasitoid had been completed (Laigo & Tamashiro 1966 and Irabagon & Brooks 1974 cited by Gröner 1986). On the other hand, individuals of the parasitoid *Hyposoter exiguae* completed their development before their hosts died of virus infection. Interestingly, if the host was exposed to the virus after parasitisation, the parasite larvae spent significantly less time in the infected host (Kaya & Tanada 1973 cited by Gröner 1986). The authors found that the parasitoid, *Apanteles militaris*, was killed or failed to pupate when its armyworm host was infected with the hypertrophic strain of an NPV.

Gröner (1990, BVL no 3683809) (reference no. IIM 8.8/11) reported that laboratory studies with several predators of lepidoptera larvae (pentatomids, lacewings, ladybirds and scavenger beetles) have demonstrated that baculoviruses pose no adverse effect, neither when fed via NPV-infected larvae, nor in consequence of their being fed baculoviral occlusion bodies suspended in semisynthetic diets, nor by contact with NPV- and GV-preparations. Furthermore, it is demonstrable that predators are potential dispersal agents of baculoviruses. This is due to the fact that they often feed on virus-infected larvae as well as on larva that have died from the effects of a baculovirus and therefore yield infectious occlusion bodies. Results from field tests suggest that the predator complex enhances the epidemic potential of baculoviruses by contaminating the foliage with occlusion bodies, either directly after individuals clean their mouthparts with the tarsi, or via faeces. Because viral occlusion bodies are retained in the gut of heteropteran nymphs which preyed on virus-diseased hosts until after the final moult, the adults (being strong fliers) appear capable of introducing the viral inoculum to healthy pest populations. Few results of studies of viral impact on adult parasites are available (Gröner 1990). Gröner (1990) summarised that baculoviruses have a narrow host range. Furthermore, no evidence of direct deleterious effects to parasites has been documented. All lethal and sublethal effects are indirect, being caused by the host's unsuitability due to virus infection. The exception is the atypical GV (synergistic)- and NPV (hypertrophic)-strain of *M. unipuncta*, which induces toxic factors in caterpillars. All lethal effects were confined to immature parasitoids developing in virus-infected hosts and decreased with increasing intervals between parasitoid oviposition and virus infection. Gröner (1990) mentioned long-term field trials investigating the effect of CpGV on the fauna of apple trees. By decimating the host population, the CpGV treatments have a notable effect on the population of codling moth parasites, in contrast to the leafroller species. Because the leafrollers were not infected by CpGV, their population level as well as that of their parasites remained unaltered, and presumably also, those of other pests (e.g., red mites and aphids) in the virus-treated plots.

Due to the narrow host range of this baculovirus (and by skipping chemical insecticides), the population of European red mites and woolly apple aphids remained below the economic threshold in the virus-treated plots. Test in Canadian apple orchards showed little effect of CpGV on populations of insects predaceous on the codling moth (thrips, clerids, pentatomids, and mirids). Numbers of the European red mite averaged around 1% of the number in chemically treated plots, providing further evidence of greater predatory activity in trees treated with CpGV.

Gröner (1990) concluded that since baculoviruses are naturally occurring, beneficial insects have always had contact with these natural regulatory agents. Deleterious effects of baculoviruses to pollinators, predators, and adult parasitoids have never been reported from nature. Atypical development of entomophagous larvae in virus-infected host larvae proved to be entirely due to the unsuitability of the host for the parasitoids in question. Host discrimination on the basis of viral infection has been documented, implying that some parasitoid species do not "waste" eggs on a host which is soon to die. Parasitoids which develop exclusively in eggs or pupae will be unaffected by or after a virus application because these stages are nearly insensitive to viral infection. The decrease in numbers of beneficial insects after pest control based on baculoviruses is due to the decreased number of hosts. In crops with a complex of pests the selective baculoviral application will allow the survival of all other insects and mites except the target pest. Therefore, alternative hosts for the predators and parasitoids are still available.

Glen et al. (1984, BVL no 3689585) (reference no. IIM 8.8/12) performed four field trials from 1978 to 1980. Sprays of codling moth granulovirus (CpGV) plus 1% skimmed milk powder did not significantly affect damage to fruit by leaf roller (tortrix moths). In laboratory tests, survival of larvae of the leaf roller *Archips podana* fed on leaves sprayed with CpGV plus milk was unaffected and they grew faster than on unsprayed leaves, because of the milk deposits. This might increase damage by *A. podana* if CpGV plus milk were applied during the feeding period of this species. In one field trial an unusual infestation of fruit by larvae of pith moth *Blastodacna atra* was not affected by CpGV. Azinphos-methyl significantly reduced damage by *B. atra* and, in one field trial where sprays were correctly timed, that by leaf rollers. CpGV had no consistently significant effects on numbers of fruit tree red spider mite *Panonychus ulmi* or its predators whereas azinphos-methyl induced outbreaks of *P. ulmi* by killing its predators.

Neuffer (1986, BVL no 2390233) (reference no. IIM 8.8/13) carried out studies of side effects of granulovirus and Insegar on the arthropod fauna in orchards of South West Germany from 1979 to 1983. Granulovirus (CpGV) is a specific biological agent for the control of the codling moth *Laspeyresia* (*Cydia*) *pomonella*. Insegar on the other hand is an insecticide, which is non neurotic but effective as a juvenilhormon analoga to control the summer fruit tree leaf roller *Adoxophyes orana*. The results achieved by beating and modified funnel methods and the fruit damage caused by arthropods evaluated at harvest time have shown that CpGV and Insegar brought good results in the control of mentioned insect, but have no significant influence on the other members of the apple tree fauna.

Bioassays with neonate larvae showed that CpGV was crossinfectious for larvae of *Cryptophlebia leucotreta* (ClGV) but it is about 1000 times less virulent than towards *C. pomonella* (Fritsch et al., 1990, BVL no 2390234; reference no. IIM 8.8/14).

According to Burges et al. (1980, BVL no 3683612) (reference no. IIM 8.8/03) NPVs proved harmless as they were unable to replicate in microorganisms, non-insect invertebrate cell lines, vertebrate cell lines, vertebrates, plants and non-arthropod invertebrates. Replication was unusual in insects outside the insect family in which the virus was first found. GVs occur only in Lepidoptera, most of them are believed to be very specific and none have replicated in cell lines from insects or other animals.

In addition, the rapidly expanding discipline of Invertebrate Pathology has failed to find incidence of NPVs and GVs infecting hosts outside the above stated host ranges. This is in reality a vast body of evidence matched only in extent by the absence of incidence of NPVs and GVs from the publications of medical, veterinary and phytopathology science.

This evidence and the accrued data from specific safety testing give increasing confidence that individual NPVs and GVs of Lepidoptera and Hymenoptera are very specific.

Successful horizontal transmission is achieved via larvae died by the CpGV-infection (Steineke, 2004, BVL no 2390213, reference no. IIIM 10.1/02). In experiments the mortality rate exceeds 40%. In contrast, the same amount of viruses applied at a spot on the surface of an apple results in a very low mortality of about 3 – 6%: It is assumed that the difference is due to the behaviour of the larvae as they show a high preference for stem and chalice. Therefore, a co-occurrence of larvae and virus is much more probable.

Conclusion:
The above mentioned literature demonstrates that there is no risk to arthropod species caused by baculoviruses and CpGV respectively.

Further literature cited

Burden, J. P., Nixon, C. P., Hodgkinson, A. E., Possee, R. D. Sait, S. M., King, L. A. & Hails, R. S. (2003). Covert infections as a mechanism for long-term persistence of baculoviruses. Ecology Letters 6, 524-531.

New information 2016

Additionally, in the literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of CpGV to non-target arthropods, one article was identified, studying the diversity of the arthropod community in apple orchards under different management strategies (Simon et al., 2007, BVL no 3306492). The aforementioned study examined the effects of codling moth management on the arthropod community and on the natural enemies of pests within apple orchards. The effect of three different regimes for the management of codling moth was assessed during a 3-year experiment on (a) the orchard performance, (b) the arthropod diversity, and (c) the structure of the complex of beneficial arthropods of both apple tree canopy and orchard grass cover, in order to provide agronomic and ecological information on the benefits and risks of each regime: supervised control of codling moth based on chemical protection (C); mating disruption against codling moth, including additional pesticides when needed (MD); and microbiological control with granulosis virus in an organic orchard (O). Infestation by *C. pomonella* and other fruit damage were assessed at 10 - 15-day intervals and at harvest by visual inspection of the fruits. The total arthropod community was studied in order to provide responses based on various taxonomic groups. At each sampling date, 50 randomly selected branches from each orchard were struck with a rubber hose over a 0.25 m diameter collection funnel. Arthropods falling from the 50 branches were collected and pooled. Seven samplings were performed each season; three before and four ding the period of pesticide application against codling moth. In the grass cover, a visual assessment was carried out prior to each sampling session in the orchard alleys to describe the plant assemblages. Plant richness was assessed in the plant assemblage covering the largest surface area. At each sampling date, a total of 70 sweeps with a 0.35 m diameter sweepnet was performed in a randomly selected place of the main plant assemblage of each orchard. Sampling was carried out twice a year, generally in May and in July, after the first and after the last pesticide application against the first generation of *C. pomonella*. For the arthropods of the apple tree canopy, the number of individuals and family richness of both non-pest and beneficial arthropods varied similarly with years in the three orchards. On the basis of the pooled number of individuals, the O orchard presented the highest number of individuals for both non-pest and beneficial arthropods, but not the richest community, since family richness was always below that of the two other orchards. Family diversity and evenness of the O orchard were always below those of both non-organic orchards which presented the same level of values. Beneficial family diversity and evenness were the highest in 2003 in both the C and MD orchards, but not the O orchard. The seasonal analysis of the number of non-pest arthropods indicated very low values in the O orchard until mid-May, then increasing values until July. In contrast, both C and MD orchards generally displayed a decrease in the number of individuals in May. The non-pest arthropod diversity tended to increase in both C and MD orchards, and the highest values were measured late June 2003 in the C orchard. For the arthropods of the grass cover, no stable tendency could be observed for the total number of individuals between May and July sampling dates in any of the three orchards, whereas the number of beneficial arthropods always increased during this period. The total and beneficial family richness tended to increase during the season from May to July in both the C and MD orchards, but remained almost constant in the O orchard. In the three orchards, phytophagous richness increased from May to July. The beneficial family diversity and evenness appeared to be less affected by the date of sampling (May or July) than the family diversity and evenness calculated on the total number of individuals. The number of individuals and the richness (total, beneficial, phytophagous) observed in the C orchard tended to be lower than in the other two orchards in 2002 and 2003, and both total and beneficial number of individuals were the highest in May in the O orchard. For both understorey and arboreal habitats, the benefit of a reduction in the intensity of codling moth management practices is therefore more in terms of biomass and functional organisation of arthropods (and potential pest control) rather than in within-orchard richness or diversity.

Cited reference:

Report: KMA 8.4/01 – Simon, S., Defrance, H., Sauphanor, B. (2007): Effect of codling moth management on orchard arthropods, published report. Agriculture, Ecosystems and Environment, 122:340-348
BVL no 3306492

Abstract: The effect of codling moth *Cydia pomonella* management on the arthropod community and on the natural enemies of pests was analysed from 2001 to 2003 in both the tree canopy and the grass cover of three experimental apple orchards under different management strategies: supervised control of codling moth based on chemical protection (C); mating disruption against codling moth, including additional pesticides when needed (MD); and microbiological control with granulosis virus in an organic orchard (O). The three management systems differed in terms of biomass and functional organisation of arthropods. Number of individuals tended to be higher in the O orchard, and the complex of beneficial arthropods of this orchard was based on polyphagous predatory arthropods (including earwigs) in both studied habitats. Conversely, parasitoid Hymenoptera constituted the prevailing group in the arboreal habitat of both the C and MD orchards. The highest diversity and evenness indices were unexpectedly measured in the C orchard. The richness of arthropods was the highest in the grass cover of the O orchard. The opposite was found in the tree canopy, the lowest values being measured in the arboreal habitat of this orchard. Depending on the year, the sampling period and the vegetation strata (apple tree canopy or grass cover), diversity and evenness indices measured in the MD orchard were either closer to the O orchard or to the C orchard.

Submitted for the purpose of renewal
Evaluation by the RMS (2020): Supplemental information.
The study investigated the effects on the arthropod community of three management systems against codling moth *Cydia pomonella*, based on chemical protection (C), mating disruption against codling moth (MD) and microbiological control with granulosis virus in an organic orchard (O).
The study demonstrated the following shortcomings:
- no control plot was used,
- artefacts due the combination of reversible population dynamics cannot be excluded,
- in the same organic orchards with an annual mean no. of 15.3 CpGV applications, several other pesticides have been used such as Copper (mean no. of 2.0 applications), Sulphur (mean no. of 12.7 applications), Rotenone (mean no. of 2.7 applications) and Mineral Oil (mean no. of 2.0 applications).
Regarding the low abundance of Hymenoptera observed in the O orchard, the study authors stated that "it is doubtful that the low abundance of Hymenoptera was related to granulosis virus applications; sulphur applications used against scab in this orchard were more likely to affect this group".
Due to the reasons above, the study is regarded as supplemental information.

B.9.5 Effects on earthworms

No data on effects of the active substance on earthworms were submitted for first valuation of the CpGV. Furthermore, no new data has been submitted for the AIR4 procedure. Instead studies on the formulated products Granulovirus CpGV SC, VIRGO and CARPOVIRUSINE were submitted for first evaluation.

An overview of the available effect data on the formulated products is given in the table below.

Test item	Test species Study design Guideline GLP status	Endpoint	Findings	Status of evaluation	Reference (Report No.; BVL-Reg.-No.)
CAR-POVIRUSINE; 1.0×10^{13} CpGV/L	*Eisenia fetida* Laboratory study OECD 207, 1984 and ISO 11268-1, 1993 GLP	Survival, body weight, signs of abnormal behaviour	No adverse effects; no visual signs of toxicity/infectivity/pathogenicity; LC_{50} > 1000 mg/kg soil dw	Already evaluated in the original DAR	Lührs, U. (2007a); 26195021; 3689741
CAR-POVIRUSINE; 1.0×10^{13} CpGV/L	*Eisenia fetida* Laboratory study OECD 222, 2004 and ISO 11268-2, 1998 GLP	Survival, body weight, feeding activity, reproduction, signs of abnormal behaviour	No adverse effects; no visual signs of toxicity/infectivity/pathogenicity; NOEC ≥ 1000 mg/kg soil dw	Already evaluated in the original DAR	Lührs, U. (2007b); 26195022; 3689742
CpGV SC; 2.2×10^{13} /L	*Eisenia foetida* Laboratory study OECD 207, 1984 and ISO 11268-1, 1993 GLP	Survival, body weight,	No adverse effects; no visual signs of toxicity/infectivity/pathogenicity; LC_{50} > 1000 mg/kg soil dw	Already evaluated in the original DAR	Wachter, S. (1998a); 96272/01-NLEf; 3687407
VIRGO; 2×10^{13} GV/L	*Eisenia foetida* Laboratory study OECD 207, 1984 and ISO 11268-1, 1993 GLP	Survival, body weight,	No adverse effects; no visual signs of toxicity/infectivity/pathogenicity; LC_{50} > 1000 mg/kg soil dw	Already evaluated in the original DAR	Colli, M. (2005d); BT013/05; 1300705

For further details, please refer to the Draft Assessment Report Volume 3, Annex B-9, point B.9.7.2 and the original dossier Annex IIIM point 10.5.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to earthworms did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

RMS conclusion:
Based on the available effect data with the formulated products in conjunction with the biological properties data (host specificity), no infectivity or pathogenicity is expected to occur in earthworms.

B.9.6 Effects on non-target soil micro-organisms

No data on effects of the active substance on non-target soil micro-organisms were submitted for first valuation of the CpGV. Furthermore, no new data has been submitted for the AIR4 procedure. Instead studies on the formulated products CpGV SC, VIRGO and CARPOVIRUSINE were submitted for first evaluation. Please refer to the Draft Assessment Report Volume 3, Annex B-9, point B.9.8.2 and the original dossier Annex IIIM point 10.6.

New information 2016

The literature search covering the last 10 years and focusing on possible toxicity or pathogenicity of *Cydia pomonella* GV to non-target soil micro-organisms did not provide any relevant information (please refer to the literature review report presented in chapter B.9.8).

B.9.7 Additional studies

The following information is derived from the Draft Assessment Report Volume 3, Annex B-9, point B.9.9. In the original dossier this information was submitted under Annex IIM point 8.11.

Resident populations of white-footed mice, *Peromyscus leucopus*, red-backed voles, *Clethrionomys gapperi*, opossums, *Didelphis marsupialis*, chipmunks, *Tamias striatus*, and racoons, *Procyon lotor*, were evaluated to detect any short term effects from aerial applications of the nucleopolyhedrovirus (NPV) of the gypsy moth (Lautenschlager et al. 1978, BVL no 3703351) (reference no. IIM 8.11/1). NPV in two formulations was sprayed on woodland plots in central Pennsylvania at the rate of 2.5×10^{12} polyhedral inclusion bodies (PIB)/ha. Comparisons of pre-spray and post-spray censuses of white-footed mice and red-backed voles in control and treated plots revealed no changes in populations or body weight that could be attributed to NPV treatments. Data from 47 caged and 250 free-living mammals showed no significant differences in organ and tissue weights, haematological values or necropsy and histopathological rankings between control and treated mammals when sample sizes were large and mean total weight between groups similar. It was concluded that aerial applications of NPV at 2.5×10^{12} PIB/ha caused no short term adverse effects to those mammals that either contacted NPV during its application or subsequently fed on NPV infected gypsy moths or other NPV-contaminated food sources.
Martignoni (1978, BVL no 3683606) (reference no. IIM 8.11/2) reported that no cytopathic effects were observed in fish and amphibian cell lines exposed to active non-occluded BV. No changes occurred in growth rate, or in the cells' response to subculture. No increase in virus titre in culture passages was demonstrable. Exposure of rainbow trout fry cells to BV failed to interfere with their susceptibility to infectious pancreatic necrosis virus. In conclusion, no evidence was found that BV is capable of entering into or altering the cells used in these studies.
Larvae of the coot clam *Mulinia lateralis* were challenged for 48h during the straight hinged stage of development with the LdMNPV (*Lymantria dispar* MNPV; MNPV = multiple nucleocapsids per virion) at a density of 106 OB/mL. Mortalities observed were significantly higher than those obtained with a control (OECD 2002, BVL no 3683046) (reference no. IIM 8.11/3).
Postlarval, early, and late juvenile stages of two species of penaeid shrimp, *Penaeus aztecus* Ives and *P. sertiferus* (L.), were tested for susceptibility to a Nucleopolyhedrovirus from *Autographa californica* (Speyer) (Lightner et al. 1973, BVL no 3683933) (reference no. IIM 8.11/4). Shrimps were exposed to the virus by intramuscular inoculation of polyhedral protein-free virus and by feeding a diet containing virus polyhedra. Mortality attributable to viral infection did not occur during the 30-day test period, nor was there histological evidence of viral segment nerve ganglia, or hypodermis.

New information 2016:

No new additional studies have been submitted in this section.

B.9.8 References relied on

Microbial pest control agent (MPCA)

Reference:	Anonymous (2016): Literature Review Report on *Cydia pomonella* Granulovirus - Effects on non-target organisms; unpublished report. BVL no 3306490
Guideline:	European Food Safety Authority; Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (OJ L 309, 24.11.2009, p. 1-50). EFSA Journal 2011;9(2):2092. [49 pp.]. doi:10.2903/j.efsa.2011.2092
GLP:	No

The data requirement "Effects on non-target organisms" was covered using a focused literature search. The notifier used the 'Scopus' database considering that:

- this database is known for being one the of the most comprehensive in the field
- an important number of references were retrieved even after removing duplicates (i.e. 4069 references)
- manual sorting of the obtained references limited the risk of excluding relevant studies.

Five separate literature searches were conducted using different search terms. A first search focused on the term *Cydia pomonella* Granulovirus and its synonyms including names of commercial products. A second search focused on baculoviruses in general but excluded search terms related to the use of these viruses for the production of recombinant proteins. In addition, some terms (Net present value, Predictive value and related terms) were excluded to limit background noise generated by the search term "NPV", abbreviation of "nucleopolyhedrovirus". Last, three searches were conducted on baculoviruses in general but focusing on specific search terms related to toxicology, ecotoxicology and fate and behaviour in the environment. Details on the used search queries are presented in Table B.9.8-2.
This strategy was used in order to avoid any bias that might result from the selection of search terms. The vast majority of relevant references were retrieved in at least two searches showing the overlapping strategy was efficient in limiting bias of search terms. The obtained references were sorted manually for relevance for the data requirements based on the criteria described below.

Table B.9.8-1: Relevance criteria for each data requirement

Data requirements according to Regulation 283/2013 part B	Criteria for relevance
"Effects on non-target organisms" (MMA Section 8)	Summary and full text assessment: 1.The article concerns a baculovirus (other viruses are not included) which has not been genetically modified 2. The article concerns the data requirement "Ecological studies, environment impact ". All test species were considered relevant (e.g. daphnids, non-target arthropods). However, tests on non-required species were considered as supporting data. No additional criteria were used for this data requirement considering the limited number of obtained references.

Table B.9.8-2: Search process for peer-reviewed open literature in bibliographic databases

	Effects on non-target organisms linked to *Cydia pomonella* Granulovirus - Details of the searches
Database:	**Scopus**
Justification for choosing the source:	Scopus is the largest abstract and citation database of peer-reviewed literature. Scopus delivers the most comprehensive overview of the world's research output in the fields of science, technology, medicine, social sciences and arts and humanities. Updated daily, Scopus contains more than 57 million records including: • Over 21,000 peer-reviewed journals • Articles-in-press (i.e., articles that have been accepted for publication) from more than 5000 international publishers • 100,000 books • 520 book series • 360 trade publications
Date of the search:	30/05/16
Date span of the search:	01/01/2005 to 30/05/16
Date of the latest database update included in the search:	30/05/16
Search strategies used for the data requirement:	
search term 1:	(TITLE-ABS-KEY (cydia AND pomonella AND granulovirus) OR TITLE-ABS-KEY (cydia AND pomonella AND gv) OR TITLE-ABS-KEY (cpgv) OR TITLE-ABS-KEY (cydia AND pomonella AND granulosis virus) OR TITLE-ABS-KEY (carpovirusine) OR TITLE-ABS-KEY (virosoft) OR TITLE-ABS-KEY (granusal) OR TITLE-ABS-KEY (madex) OR TITLE-ABS-KEY (virin) OR TITLE-ABS-KEY (cyap) OR TITLE-ABS-KEY (carpovirus AND plus) OR TITLE-ABS-KEY (cyd-x) OR TITLE-ABS-KEY (carpostop) OR TITLE-ABS-KEY ("Evo 2") OR TITLE-ABS-KEY (carpo 600) OR TITLE-ABS-KEY (virgo AND *virus)) AND PUBYEAR > 2005
search term 2:	(TITLE-ABS-KEY (baculovirus) OR TITLE-ABS-KEY (Baculoviridae) OR TITLE-ABS-KEY (nucleopolyhedrovirus) OR TITLE-ABS-KEY (nuclear AND polyhedrosis AND virus) OR TITLE-ABS-KEY (npv) OR TITLE-ABS-KEY (granulovirus) OR TITLE-ABS-KEY (Betabaculovirus) AND NOT (TITLE-ABS-KEY (Net present value) OR TITLE-ABS-KEY (Protein expression) OR TITLE-ABS-KEY (Diagnostic test accuracy study) OR TITLE-ABS-KEY (Recombinant Proteins) OR TITLE-ABS-KEY (Baculovirus expression system) OR TITLE-ABS-KEY (Gene expression) OR TITLE-ABS-KEY (Predictive value) OR TITLE-ABS-KEY (Predictive value) OR TITLE-ABS-KEY (Predictive Value of Tests) OR TITLE-ABS-KEY (Diagnostic accuracy) OR TITLE-ABS-KEY ("Diagnostic value")))AND PUBYEAR > 2005
search term 3:	(TITLE-ABS-KEY (baculovirus) OR TITLE-ABS-KEY (Baculoviridae) OR TITLE-ABS-KEY (nucleopolyhedrovirus) OR TITLE-ABS-KEY (nuclear AND polyhedrosis AND virus) OR TITLE-ABS-KEY (npv) OR TITLE-ABS-KEY (granulovirus) OR TITLE-ABS-KEY (Betabaculovirus) AND NOT (TITLE-ABS-KEY (Net present value)))AND PUBYEAR > 2005 AND (TITLE-ABS-KEY (beneficial) OR TITLE-ABS-KEY (non target) OR TITLE-ABS-KEY (predator) OR TITLE-ABS-KEY (parasitoid) OR TITLE-ABS-KEY (pollinator))
search term 4:	(TITLE-ABS-KEY (baculovirus) OR TITLE-ABS-KEY (Baculoviridae) OR TITLE-ABS-KEY (nucleopolyhedrovirus) OR TITLE-ABS-KEY (nuclear AND polyhedrosis AND virus) OR TITLE-ABS-KEY (npv) OR TITLE-ABS-KEY (granulovirus) OR TITLE-ABS-KEY (Betabaculovirus) AND NOT (TITLE-ABS-KEY (Net present value)))AND PUBYEAR > 2005 AND (TITLE-ABS-KEY (toxicity) OR TITLE-ABS-KEY (mammals) OR TITLE-ABS-KEY (rat) OR TITLE-ABS-KEY (pathogenicity) OR TITLE-ABS-KEY (infectivity))
search term 5:	(TITLE-ABS-KEY (baculovirus) OR TITLE-ABS-KEY (baculoviridae) OR TITLE-ABS-KEY (nucleopolyhedrovirus) OR TITLE-ABS-KEY (nuclear AND

	polyhedrosis AND virus) OR TITLE-ABS-KEY (npv) OR TITLE-ABS-KEY (granulovirus) OR TITLE-ABS-KEY (betabaculovirus)) AND PUBYEAR > 2005 AND (TITLE-ABS-KEY (persistence) OR TITLE-ABS-KEY (soil) OR TITLE-ABS-KEY (water) OR TITLE-ABS-KEY (uv) OR TITLE-ABS-KEY (transport)) AND NOT (TITLE-ABS-KEY (net present value))
Total number of summary records retrieved:	5078
Total number of summary records retrieved after removing duplicates	4069

A very broad literature search was conducted in the "Scopus" database based on five separate literature searches using different search terms. This resulted in a high number of references. A total of 4069 reference was retrieved for all data requirements. However, many of these references do not concern the data requirements. After manual sorting of the references, based on the criteria presented in Table 9.8-1, a total of 41 references was selected for full text assessment for Effects on human health (14), Fate and behaviour in the environment (15) and Effects on non-target organisms (12). Based on full text evaluation a total of 31 studies was considered irrelevant for Effects on human health, Fate and behaviour in the environment and Effects on non-target organisms.

Table B.9.8-3: Results of the study selection process

Data requirement captured in the search (as indicated in Table 9.8-2)	n
Total number of summary records retrieved after all searches of peer-reviewed literature (excluding duplicates)	4069
Number of summary records excluded from search results after rapid assessment of relevance	4028
Total number of full-text documents assessed in detail (in total for Effects on human health, Fate and behaviour in the environment and Effects on non-target organisms)	41
Number of studies excluded from further consideration after detailed assessment of relevance	31
Number of studies not excluded from further consideration after detailed assessment of relevance (i.e. relevant studies and studies of unclear relevance) in total for Effects on human health, Fate and behaviour in the enviruonment and Effects on non-target organisms	10
Number of studies not excluded from further consideration after detailed assessment of relevance (i.e. relevant studies and studies of unclear relevance) for the data requirement "Effects on non-target organisms"	2

Table B.9.8-4: Studies excluded from the risk assessment after detailed assessment of full-text documents

Author	Year	Title	Source	Reason(s) for not including this study in the dossier
Ansari S, Ahmad, S., Ahmad N., Ahmad T., Hasan, F	2013	Microbial insecticides: Food security and human health (Book Chapter)	A. Malik et al. (eds.), Management of Microbial Resources in the Environment	No relevant information is given about Baculoviruses. The focus of this review is on other microbial insecticides.
Arthurs S. P.,	2007	Evaluation of the codling moth	Biological	The article was

Lacey L. A. and Miliczky E. R.		granulovirus and spinosad for codling moth control and impact on non-target species in pear orchards	Control 41 (1): 99-109	rejected because the focus is on efficacy and not on non-target organisms.
Fuxa J.; Richter A.	2007	Effect of nucleopolyhedrovirus concentration in soil on viral transport to cotton (*Gossypium hirsutum* L.) plants	BioControl (2007) 52:821–843	The article was rejected because it concerns a recombinant nucleopolyhedrovirus
Fuxa J.; Richter A.; Milks M.	2007	Threshold distances and depths of nucleopolyhedrovirus in soil for transport to cotton plants by wind and rain	Journal of Invertebrate Pathology 95 (2007) 60–70	The article was rejected because it concerns a recombinant nucleopolyhedrovirus
Fuxa J	2008	Threshold Concentrations of Nucleopolyhedrovirus in Soil to Initiate Infections in *Heliothis virescens* on Cotton Plants	Microb Ecol (2008) 55:530–539	The article was rejected because it concerns a recombinant nucleopolyhedrovirus
Garantonakis N., Varikou K. and Birouraki A.	2016	Comparative selectivity of pesticides used in greenhouses, on the aphid parasitoid *Aphidius colemani* (Hymenoptera: Braconidae)	Biocontrol Science and Technology 26 (5): 678-690	The article was rejected because the focus is on efficacy and not on non-target organisms.
Kalawate A.	2014	Microbial Viral Insecticides	K. Sahayaraj (ed.), Basic and Applied Aspects of Biopesticides,	The article was selected because ultraviolet light (degradation) is mentioned in the abstract. However, the full text publication only concerns history, genome and commercial products.
Lacey L., Kroschel J., Arthurs S., De La Rosa F.	2010	Microbial Control of the Potato Tuber Moth *Phthorimaea operculella* (Lepidoptera: Gelechiidae)	Revista Colombiana de Entomología 36 (2): 181-189 (2010)	The article was selected because non-target organisms and human health are mentioned in the abstract. However, the full text publication only concerns efficacy and virus biology.
Moore, S.D., Hendry, D.A., Richards, G.I.	2011	Virulence of a South African isolate of the *Cryptophlebia leucotreta* granulovirus to Thaumatotibia leucotreta neonate larvae	BioControl, Volume 56, Issue 3, June 2011, Pages 341-352	The article was selected because isolation of a viral strain from the environment was mentioned in the abstract. However, the strain was not isolated for the natural environment but from a laboratory contamination. The

				article is thus irrelevant to the data requirement “natural occurrence”.
Stefanovska T., Pidlisnyuk V., Kaya H.	2006	Biological control of pests in Ukraine: legacy from the past and challenges for the future	CAB Reviews: Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources 2006 1, No. 008	The article was selected because non-target organisms are mentioned in the abstract. However, the full text publication only concerns efficacy and use history.

Table B.9.8-5: Relevant studies subjected to a detailed assessment of full-text documents (n = 2) by data requirement

Data requirement (numbered according to Regulation 283/2013 part B)	Author(s)	Year	Title	Source
8. EFFECTS ON NON-TARGET ORGANISMS				
8.3. Effects on bees				
8.3	Mommaerts V., Sterk G., Hoffmann L. and Smagghe G.	2009	A laboratory evaluation to determine the compatibility of microbiological control agents with the pollinator *Bombus terrestris*	Pest Management Science 65 (9): 949-955
8.4. Effects on arthropods other than bees				
8.4	Simon S., Defrance H. and Sauphanor B.	2007	Effect of codling moth management on orchard arthropods	Agriculture, Ecosystems and Environment 122 (3): 340-348

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8/01	Anonymous	2016	LITERATURE REVIEW REPORT ON CYDIA POMONELLA GRANULOVIRUS - EFFECTS ON NON-TARGET ORGANISMS Arysta LifeScience S.A.S., not applicable not available GLP/GEP: no Published: no 3306490	no	yes	New data for active ingredient, not previously submitted nor evaluated	ALS	N
KMA 8.1	Ignoffo, C.M.	1975	EVALUATION OF IN VIVO SPECIFICITY OF INSECT VIRUSES not available, not applicable In: Baculoviruses for insect pest control: Safety considerations ... Publisher: American Society for Microbiology, 52-57 GLP/GEP: no Published: yes 3683296	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Martignoni, M.E.	1978	THE DOUGLAS-FIR TUSSOCK MOTH: A SYNTHESIS not available, not applicable Forest Ser. Tech. Bulletin 1585. U.S. Dep. of Agriculture, ed. by: Brookes, M.H., Stark, R.W., Campell, R.W. GLP/GEP: no Published: yes 3683297	no	no	not protected	-	Y KIIM 8.1

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.1	Lautenschlager, R.A., Rothenbacher, H., Podgwaite, J.D.	1979	RESPONSE OF BIRDS TO AERIAL APPLICATION OF THE NUCLEOPOLYHEDROSIS VIRUS OF THE GYPSY MOTH, LYMANTRIA DISPAR not available, not applicable Environ. Entomol. 8, pp. 760-764 GLP/GEP: no Published: yes 3683299	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Burges, H.D., Croizier, G., Huber, J.	1980	A REVIEW OF SAFETY TESTS ON BACULOVIRUSES not available, not applicable Entomophaga 25 (4), 329-339 GLP/GEP: no Published: yes 3683298	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Lewis, F.B., Podgwaite, J.D.	1981	THE GYPSY MOTH: RESEARCH TOWARD INTEGRATED PEST MANAGEMENT - SAFETY EVALUATIONS not available, not applicable Technical Bulletin, U.S. Department of Agricultur, 1584, 475-479 GLP/GEP: no Published: yes 3683300	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Burges, H.D.	1981	MICROBIAL CONTROL OF PESTS AND PLANT DISEASES 1970-1980 not available, not applicable Microbial control of pests and plant diseases, Academic Press, pp. 392-393, ed. Burges H.D. GLP/GEP: no Published: yes 3683570	no	no	not protected	-	Y KIIM 8.1

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.1	Gröner, A., Döller, G.	1982	PASSAGE OF INFECTIOUS NUCLEAR POLYHEDROSIS VIRUS BY MICE AND CHICKENS not available, not applicable Entomophagna 27 (2), 155-157 GLP/GEP: no Published: yes 3683303	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Xuebao, W.	1982	SAFETY TESTS OF A GV INSECTICIDE AGAINST CABBAGE BUTTERFLY PIERIS RAPAE LARVAE not available, not applicable RAE Serie A, 70 (4), 2368 GLP/GEP: no Published: yes 3683558	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Gröner, A.	1990	SAFETY TO NONTARGET INVERTEBRATES OF BACULOVIRUSES not available, not applicable Safety of microbial insecticides, Laird M., Lacey L.A., Davidson E.W., Chapter 10, 135-147 GLP/GEP: no Published: yes 3683559	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Lautenschlager, R.A., Podgwaite, J.D., Watson, D.E.	1980	NATURAL OCCURRENCE OF THE NUCLEOPOLYHEDROSIS VIRUS OF THE GYPSY MOTH, LYMANTRIA DISPAR (LEP.: LYMANTRIIDAE) IN WILD BIRDS AND MAMMALS not available, not applicable Entomophaga, 25 (3), 261-267 GLP/GEP: no Published: yes 3683560	no	no	not protected	-	Y KIIM 8.1

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.1	Entwistle, P.F., Adams, P.H.W., Evans, H.F.	1978	EPIZOOTIOLOGY OF A NUCLEAR POLYHEDROSIS VIRUS IN EUROPEAN SPRUCE SAWFLY (GILPINIA HERCYNIAE): THE RATE OF PASSAGE OF INFECTIVE VIRUS THROUGH THE GUT OF BIRDS DURING CAGE TESTS not available, not applicable Journal of Invertebrate Pathology 31, 307-312, 1978 GLP/GEP: no Published: yes 3683561	no	no	not protected	-	Y KIIM 8.1
KMA 8.1	Gröner, A.	1986	SPECIFICITY AND SAFETY OF BACULOVIRUSES not available, not applicable The Biology of Baculoviruses, Volume I, Biological Properties and Molecular Biologie, Chapter 9, 177-201 GLP/GEP: no Published: yes 3683563	no	no	not protected	-	Y KIIM 8.1
KMA 8.2.1	Banowetz, G.M., Fryer, J.L., Iwai P.J., Martignoni, M.E.	1976	EFFECTS OF THE DOUGLAS-FIR TUSSOCK MOTH NUCLEOPOLYHEDROSIS VIRUS (BACULOVIRUS) ON THREE SPECIES OF SALMONID FISH not available, not applicable USDA Forest Service Research Paper-PNW 214 GLP/GEP: no Published: yes 3683920	no	no	not protected	-	Y KIIM 8.2

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.2.1	Gröner, A., Huber, J., Krieg, A.	1981	USE OF BACULOVIRUSES IN CROP PROTECTION: SAFETY TO AQUATIC ORGANISMS (GERMAN ORIGINAL) not available, not applicable Z Binnenfischerei, 31 (4), 25-27 GLP/GEP: no Published: yes 3683565	no	no	not protected	-	Y KIIM 8.2
KMA 8.2.1	Gröner, A.	1986	SPECIFICITY AND SAFETY OF BACULOVIRUSES not available, not applicable The Biology of Baculoviruses, Volume I, Biological Properties and Molecular Biologie, Chapter 9, 177-201 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683912	no	no	not protected	-	Y KIIM 8.2
KMA 8.2.1	Gröner, A.	1990	SAFETY TO NONTARGET INVERTEBRATES OF BACULOVIRUSES not available, not applicable Safety of microbial insecticides, Laird M., Lacey L.A., Davidson E.W., Chapter 10, 135-147 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683806	no	no	not protected	-	Y KIIM 8.2

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.2.1	Hicks, B.D., Geraci, J.R., Cunningham, J.C., Arif, B.M.	1981	EFFECTS OF RED-HEADED PINE SAWFLY, NEODIPRION LECONTEI, NUCLEAR POLYHEDROSIS VIRUS ON RAINBOW TROUT, SALMO GAIRDNERI AND DAPHNIA PULEX not available, not applicable J. Environ. SCI. Health, B16 (4), pp. 493-509 GLP/GEP: no Published: yes 3683926	no	no	not protected	-	Y KIIM 8.2
KMA 8.2.1	Burges, H.D., Croizier, G., Huber, J.	1980	A REVIEW OF SAFETY TESTS ON BACULOVIRUSES not available, not applicable Entomophaga 25 (4), 329-339 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683610	no	no	not protected	-	Y KIIM 8.2
KMA 8.2.1	Burges, H.D.	1981	MICROBIAL CONTROL OF PESTS AND PLANT DISEASES 1970-1980 not available, not applicable Microbial control of pests and plant diseases, Academic Press, pp. 392-393, ed. Burges H.D. GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683301	no	no	not protected	-	Y KIIM 8.2

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.2.1	Lewis, F.B., Podgwaite, J.D.	1981	THE GYPSY MOTH: RESEARCH TOWARD INTEGRATED PEST MANAGEMENT - SAFETY EVALUATIONS not available, not applicable Technical Bulletin, U.S. Department of Agricultur, 1584, 475-479 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683800	no	no	not protected	-	Y KIIM 8.2
KMA 8.2.1	Xuebao, W.	1982	SAFETY TESTS OF A GV INSECTICIDE AGAINST CABBAGE BUTTERFLY PIERIS RAPAE LARVAE not available, not applicable RAE Serie A, 70 (4), 2368 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683905	no	no	not protected	-	Y KIIM 8.2
KMA 8.2.1	Ignoffo, C.M.	1975	EVALUATION OF IN VIVO SPECIFICITY OF INSECT VIRUSES not available, not applicable In: Baculoviruses for insect pest control: Safety considerations ... Publisher: American Society for Microbiology, 52-57 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683600	no	no	not protected	-	Y KIIM 8.2

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.2.1	Ashour, M.B., Ragheb, D.A., El-Sheikh, E.S.A., Gomaa, E.A.A., Kamita, S.G., Hammock, B.D.	2007	BIOSAFETY OF RECOMBINANT AND WILD TYPE NUCLEOPOLYHEDROVIRUSES AS BIOINSECTICIDES not available, not applicable International Journal of Environmental Research and Public Health, 4(2), 111-125 GLP/GEP: no Published: yes 3306476	no	no	not protected	-	N
KMA 8.2.1	Kreutzweiser D.P., Ebling P.M., Holmes S.B.	1997	INFECTIVITY AND EFFECTS OF GYPSY MOTH AND SPRUCE BUDWORM NUCLEAR POLYHEDROSIS VIRUSES INGESTED BY RAINBOW TROUT. not available, not applicable Ecotoxicology and Environmental Safety, 38(1), 63-70 GLP/GEP: no Published: yes	no	no	not protected	-	N
KMA 8.2.2	Copping, L.G.	2001	CYDIA POMONELLA GRANULOSIS VIRUS not available, not applicable The BioPesticide Manual, pp. 60-61 GLP/GEP: no Published: yes 3683588	no	no	not protected	-	Y KIIM 8.3
KMA 8.2.2	Gröner, A.	1986	SPECIFICITY AND SAFETY OF BACULOVIRUSES not available, not applicable The Biology of Baculoviruses, Volume I, Biological Properties and Molecular Biologie, Chapter 9, 177-201 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683913	no	no	not protected	-	Y KIIM 8.3

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.2.2	Gröner, A.	1990	SAFETY TO NONTARGET INVERTEBRATES OF BACULOVIRUSES not available, not applicable Safety of microbial insecticides, Laird M., Lacey L.A., Davidson E.W., Chapter 10, 135-147 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683807	no	no	not protected	-	Y KIIM 8.3
KMA 8.2.2	Hicks, B.D., Geraci, J.R., Cunningham, J.C., Arif, B.M.	1981	EFFECTS OF RED-HEADED PINE SAWFLY, NEODIPRION LECONTEI, NUCLEAR POLYHEDROSIS VIRUS ON RAINBOW TROUT, SALMO GAIRDNERI AND DAPHNIA PULEX not available, not applicable J. Environ. SCI. Health, B16 (4), pp. 493-509 GLP/GEP: no Published: yes **Submitted in: KMA 8.2.1** 3683926	no	no	not protected	-	Y KIIM 8.3
KMA 8.2.2	Burges, H.D., Croizier, G., Huber, J.	1980	A REVIEW OF SAFETY TESTS ON BACULOVIRUSES not available, not applicable Entomophaga 25 (4), 329-339 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683611	no	no	not protected	-	Y KIIM 8.3

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.2.2	Lewis, F.B., Podgwaite, J.D.	1981	THE GYPSY MOTH: RESEARCH TOWARD INTEGRATED PEST MANAGEMENT - SAFETY EVALUATIONS not available, not applicable Technical Bulletin, U.S. Department of Agricultur, 1584, 475-479 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683801	no	no	not protected	-	Y KIIM 8.3
KMA 8.3/01	Mommaerts, V., Sterk, G., Hoffmann, L., Smagghe, G.	2009	A LABORATORY EVALUATION TO DETERMINE THE COMPATIBILITY OF MICROBIOLOGICAL CONTROL AGENTS WITH THE POLLINATOR BOMBUS TERRESTRIS not available, not applicable Pest Management Science, 65, 949-955 GLP/GEP: no Published: yes 3306491	no	no	not protected	-	N
KMA 8.3	Gröner, A., Huber, J., Krieg, A., Pinsdori, W.	1978	BIENENPRÜFUNG VON ZWEI BACULOVIRUS PRÄPARATEN Nachrichtenbl. Deut. Flanzenschutzd., 30, 3, 39-41. GLP/GEP: no/no Published: yes 2019293	no	no	not protected	-	Y KIIM 8.7
KMA 8.3	Knox, D.A	1970	TESTS OF CERTAIN INSECT VIRUSES ON COLONIES OF HONEYBEES. J. invertebr. Pathol. 16, 152 GLP/GEP: no/no Published: yes 3689576	no	no	not protected	-	Y KIIM 8.7

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.3	Cantwell G.E., Knox D.A., Lehnert T., Michael A.S.	1966	MORTALITY OF THE HONEY BEE, APIS MELLIFERA, IN COLONIES TREATED WITH CERTAIN BIOLOGICAL INSECTICIDES J Invertebr Pathol. 8, 228-233 GLP/GEP: no/no Published: yes	no	no	not protected	-	N
KMA 8.3	Copping, L.G.	2001	CYDIA POMONELLA GRANULOSIS VIRUS not available, not applicable The BioPesticide Manual, pp. 60-61 GLP/GEP: no Published: yes 1300650 / BIE2006-65	no	no	not protected	-	Y KIIM 8.7
KMA 8.3	Gröner, A.	1990	SAFETY TO NONTARGET INVERTEBRATES OF BACULOVIRUSES not available, not applicable Safety of microbial insecticides, Laird M., Lacey L.A., Davidson E.W., Chapter 10, 135-147 GLP/GEP: no Published: yes 1300651 / BIE2006-121	no	no	not protected	-	Y KIIM 8.7
KMP 10.3	Schmitzer, S.	2006	EFFECTS OF CARPOVIRUSINE (ACUTE CONTACT AND ORAL) ON HONEY BEES (APIS MELLIFERA L.) IN THE LABORATORY Arysta LifeScience S.A.S., 26194035 Institut für Analytik u. Umweltchemie GmbH, Germany GLP: yes Published: no 3689722	no	no	not protected	ALS	Y KIIIM 10.3

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMP 10.3	Colli, M.	2005	SIDE EFFECTS (ACUTE ORAL AND CONTACT TOXICITY) OF VIRGO ON THE HONEY BEE, APIS MELLIFERA L., IN LABORATORY (LIMIT TEST). Sipcam S.p.A., BT008/05 Biotecnologie BT Srl, Fraz. Pantalla, Italy GLP: yes Published: no 1300695 / BIE2006-68	no	no	not protected	SIP	Y KIII M 10.3
KMP 10.3	Kling, A.	2002	ASSESSMENT OF SIDE EFFECTS OF GRANUPOM TO THE HONEY BEE, APIS MELLIFERA L. IN THE LABORATORY Andermatt Biocontrol GmbH / Probis GmbH, 20011323/01-BLEU ArGe GAB Biotech/IFU, Niefern-Öschelbronn, Germany GLP: yes Published: no 1914013	no	no	not protected	PKA	Y KIII M 10.3
KMA 8.4	Copping, L.G.	2001	CYDIA POMONELLA GRANULOSIS VIRUS not available, not applicable The BioPesticide Manual, pp. 60-61 GLP/GEP: no Published: yes **Submitted in: KMA 8.2.2** 3683590	no	no	not protected	-	Y KIIM 8.8

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.4	Ignoffo, C.M.	1975	EVALUATION OF IN VIVO SPECIFICITY OF INSECT VIRUSES not available, not applicable In: Baculoviruses for insect pest control: Safety considerations ... Publisher: American Society for Microbiology, 52-57 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683601	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Burges, H.D., Croizier, G., Huber, J.	1980	A REVIEW OF SAFETY TESTS ON BACULOVIRUSES not available, not applicable Entomophaga 25 (4), 329-339 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683612	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Huber, J.	1978	ABOUT THE HOST SPECTRUM OF THE CODLING MOTH GRANULOSIS VIRUS not available, not applicable Safety aspects of baculoviruses as Biological Insecticides, 75-85 GLP/GEP: no Published: yes 3683575	no	no	not protected	-	Y KIIM 8.8

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.4	Jaques, R.P., Laing, J.E., MacLellan, C.R.,Proverbs, M.D., Sanford, K.H., Trottier, R.	1981	APPLE ORCHARD TESTS ON THE EFFICACY OF THE GRANULOSIS VIRUS OF THE CODLING MOTH, LASPEYRESIA POMONELLA [LEP.: OLETHREUTIDAE] not available, not applicable Entomophaga 26 (2), pp. 111-118 GLP/GEP: no Published: yes 3683576	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Dickler, E.	1986	EINFLUSS VON BEHANDLUNGEN MIT APFELWICKLER-GRANULOSEVIRUS (CPGV) UND BREITENWIRKSAMEN CHEMISCHEN INSEKTIZIDEN AUF PARASITEN DES APFELWICKLERS UND PARASITEN VON SCHALENWICKLERARTEN not available, not applicable Biologische Bundesanstalt, Inst. f. Pflanzenschutz im Obstbau, Dossenheim, 90-97 GLP/GEP: no Published: yes 3683578	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Huber, J.	1995	PRELIMINARY TESTS FOR USE OF THE GRANULOSIS VIRUS OF THE CODLING MOTH FOR CONTROL OF THE EUROPEAN PINE SHOOT MOTH not available, not applicable Mod Meth z Bek von Schadinsekten, 2, 59-64 GLP/GEP: no Published: yes 3683579	no	no	not protected	-	Y KIIM 8.8

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.4	Lewis, F.B., Podgwaite, J.D.	1981	THE GYPSY MOTH: RESEARCH TOWARD INTEGRATED PEST MANAGEMENT - SAFETY EVALUATIONS not available, not applicable Technical Bulletin, U.S. Department of Agricultur, 1584, 475-479 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683803	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Xuebao, W.	1982	SAFETY TESTS OF A GV INSECTICIDE AGAINST CABBAGE BUTTERFLY PIERIS RAPAE LARVAE not available, not applicable RAE Serie A, 70 (4), 2368 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683906	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Gröner, A.	1986	SPECIFICITY AND SAFETY OF BACULOVIRUSES not available, not applicable The Biology of Baculoviruses, Volume I, Biological Properties and Molecular Biologie, Chapter 9, 177-201 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683915	no	no	not protected	-	Y KIIM 8.8

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.4	Gröner, A.	1990	SAFETY TO NONTARGET INVERTEBRATES OF BACULOVIRUSES not available, not applicable Safety of microbial insecticides, Laird M., Lacey L.A., Davidson E.W., Chapter 10, 135-147 GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683809	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Glen, D.M., Wiltshire, C.W., Milsom, N.F., Brain, P.	1984	CODLING MOTH GRANULOSIS VIRUS: EFFECTS OF ITS USE ON SOME OTHER ORCHARD ARTHROPODS not available, not applicable Annals of Applied Biology, 104, 99-106 GLP/GEP: no Published: yes 3689585	no	no	not protected	-	Y KIIM 8.8
KMA 8.4	Neuffer, G.	1986	ZUR FRAGE VON NEBENWIRKUNGEN VON GRANULOSE-VIRUS UND INSEGAR AUF DIE ARTHROPODENFAUNE IN APFELANLAGEN SÜDWESTDEUTSCHLANDS not available, not applicable Symposium integrated plant protection in orchards, 118-123 GLP/GEP: no Published: yes 2390233	no	no	not protected	-	Y KIIM 8.8

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.4	Fritsch, E., Huber, J., Backhaus, H.	1990	CPGV AS A TOOL IN THE RISK ASSESSMENT OF GENETICALLY ENGINEERED BACULOVIRUSES not available, not applicable Vth International Colloque on Invertebrate Pathology and Microbial Control, Adelaide, Australia, 439-443 GLP/GEP: no Published: yes 2390234	no	no	not protected	-	Y KIIM 2.4
KMA 8.4	Steineke, S.B.	2004	POPULATIONSDYNAMIK DES CYDIA POMONELLA GRANULOVIRUS not available, not stated Johannes Gutenberg-Universität, Fachbereich Biologie, Mainz GLP/GEP: no Published: no 2390213	no	no	not protected		Y KIIM 7.1
KMA 8.4/01	Simon, S., Defrance, H., Sauphanor, B.	2007	EFFECT OF CODLING MOTH MANAGEMENT ON ORCHARD ARTHROPODS not available, not applicable Agriculture, Ecosystems and Environment, 122, 340-348 GLP/GEP: no Published: yes 3306492	no	no	not protected	-	N

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KMA 8.7	Lautenschlager, R.A., Rothenbacher, H., Podgwaite, J.D.	1978	RESPONSE OF SMALL MAMMALS TO AERIAL APPLICATIONS OF THE NUCLEOPOLYHEDROSIS VIRUS OF THE GYPSY MOTH, LYMANTRIA DISPAR not available, not applicable Environ Entomol, 7, 676-683 GLP/GEP: no Published: yes 3703351	no	no	not protected	-	Y KIIM 8.11
KMA 8.7	Martignoni, M.E.	1978	THE DOUGLAS-FIR TUSSOCK MOTH: A SYNTHESIS not available, not applicable Forest Ser. Tech. Bulletin 1585. U.S. Dep. of Agriculture, ed. by: Brookes, M.H., Stark, R.W., Campell, R.W. GLP/GEP: no Published: yes **Submitted in: KMA 8.1** 3683606	no	no	not protected	-	Y KIIM 8.11
KMA 8.7	OECD	2002	CONSENSUS DOCUMENT ON INFORMATION USED IN THE ASSESSMENT OF ENVIRONMENTAL APPLICATIONS INVOLVING BACULOVIRUS not available, not applicable ENV/JM/MONO, 1, 1-90 GLP/GEP: no Published: yes 3683046	no	no	not protected	-	Y KIIM 8.11

Data point	Author(s)	Year	Title Owner, Report No. Source (where different from owner) GLP or GEP status Published or not BVL registration number	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previously submitted Y/N* If Y => old data point
KMA 8.7	Lightner, D.V., Proctor, R.R., Sparks, A.K.,Adams, J.R.,Heimpel, A.M.	1973	TESTING PENAEID SHRIMP FOR SUSCEPTIBILITY TO AN INSECT NUCLEAR POLYHEDROSIS VIRUS not available, not applicable Environm. Entomol., 2, p. 611-613 GLP/GEP: no Published: yes 3683933	no	no	not protected	-	Y KIIM 8.11