List of end points

Rapporteur Member State	Month and year	Microbial or Viral Agent (Name)
Germany	**October 2020**	***Cydia pomonella* GV**

Identity, Biological properties, Details of uses, Further information, and Proposed Classification and Labelling

Active microorganism:	*Cydia pomonella* Granulovirus (CpGV)
Function (*e.g.* control of fungi):	Insecticide
Rapporteur Member State:	Germany
Co-rapporteur Member State:	The Netherlands
Identity of the Microbial or Viral Agent used in plant protection / Active Substance) (Regulation (EU) N° 283/2013, Annex Part B, point 1)	
Name of the organism:	*Cydia pomonella* granulovirus (CpGV)
Taxonomy:	Family: Baculoviridae Genus: Betabaculovirus
Species, subspecies, strain:	*Cydia pomonella* Granulovirus Several isolates
Identification / detection:	The identity of the virus produce can be bioanalytically checked against the other isolates by - SDS-polyacrylamide-gel electrophoresis of the virus proteins - Restriction endonuclease analysis of viral DNA
Culture collection:	<u>Andermatt Biocontrol GmbH</u> All isolates are deposited in the German Collection of Microorganisms and Cell Cultures (DSMZ), Inhoffenstraße 7B, D-38124 Braunschweig, Germany. Mexican isolate: Virus accession number: GV-0001 CpGV-V01: Virus accession number: GV-0003 CpGV-V03: Virus accession number: GV-0006 CpGV-V15: Virus accession number: GV-0013 CpGV-V22: Virus accession number: GV-0014 CpGV-V14: Virus accession number: GV-0015 CpGV-V45: Virus accession number: GV-0017 <u>Arysta LifeScience S.A.S.</u> All isolates are deposited in the German Collection of Microorganisms and Cell Cultures (DSMZ), Inhoffenstraße 7B, D-38124 Braunschweig, Germany. Mexican isolate: Virus accession number: GV-0002 CpGV-R5 Virus accession number: GV-0007

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Minimum and maximum concentration of the MPCA used for manufacturing of the formulated product (cfu; g/kg):	Andermatt Biocontrol GmbH Content of CpGV: 6.0 x 10^{13} granules/L min 6 × 10^{13} granules/L, max 12 × 10^{13} granules/L Arysta LifeScience S.A.S. Minimal CpGV concentration: 2.6 x 10^{13} granules/L Nominal CpGV concentration: 3.2 x 10^{13} granules/L Maximal CpGV concentration: 1.8 x 10^{14} granules/L Serbios srl No own isolate is produced.
Identity and content of relevant impurities, additives, contaminating organisms in the technical grade of MPCA:	*Bacillus cereus*: < 1 × 10^{7} CFU/g in the formulated product
Is the MPCA genetically modified; if so provide type of modification	Not applicable

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Rapporteur Member State	Month and year	Microbial or Viral Agent (Name)
Germany	**October 2020**	***Cydia pomonella* GV**

Biological properties of the microorganism (Regulation (EU) N° 283/2013, Annex Part B, point 2)

Origin and natural occurrence, Background level:	CpGV has been isolated from codling moth larvae on apple and pear trees found in Mexico (near Valle de Allende, Chihuahua). CpGV is ubiquitous in the environment. Its geographic distribution corresponds with the distribution of its hosts. Not known
Target organism(s):	Larvae of the codling moth *Cydia pomonella* (all CpGV isolates, i.e. CpGV-M, CpGV-V01, CpGV-V03, CpGV-V15, CpGV-V22, CpGV-V45, and CpGV-R5) larvae of the oriental fruit moth *Grapholita molesta* (CpGV-R5, CpGV-V22 and CpGV-V45)
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 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. The body of the insect liquefies and the virus is released into the environment where it can infect other codling moth and oriental fruit moth larvae. 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:	CpGV acts highly specific against larvae of the codling moth *Cydia pomonella* and some isolates can infest the oriental fruit moth *Grapholita molesta* and the plum fruit moth *Grapholita funebrana*. In addition cross transmission experiments have revealed alternative hosts of the tortricid family of the Lepidoptera for CpGV. Not pathogenic to humans / mammals / plants.
Life cycle:	The natural route of infection is the peroral ingestion of viral occlusion bodies by larvae. In the alkaline environment of the midgut, the occlusion bodies dissolve rapidly and occlusion-derived virions (ODV's) are released. The ODV's pass through the peritrophic membrane of the midgut. After attachment to the microvilli of the midgut epithelium, the nucleocapsids enter the cell lumen. The nucleocapsids are transported to the nucleus, the viral DNA is released, and DNA expression and replication is initiated. Initial replication produces non-occluded virus particles. By exocytosis the newly formed virions get to the hemolymph and from there into various tissues of the organism. After cell lysis a large number of occluded CpGV is set free which are then capable to infest new hosts.
Infectivity, dispersal and colonisation ability:	The persistence of CpGV on leaves/fruits is mainly delimited by sunlight. The calculated half-lives of CpGV due to UV-irradiation range from 15 to 52 sunlight hours. However, while about 99% of CpGV is rather quickly inactivated, a small portion of CpGV persists much longer. In soil CpGV will persist for longer periods than on leaves/fruits. In soil persistence of CpGV is mainly regulated by the soil pH: the lower the pH, the more rapidly the virus is inactivated. Little is known regarding the persistence of CpGV in natural aquatic environments. However, it is supposed that the pH and the salt

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	concentration of the water influence its stability. CpGV can be stored for two years at 5-8°C without losing any activity, however, it loses its efficacy if stored at temperatures above 54°C for more than 14 days, indicating that CpGV will likely also persist in the environment at lower temperatures but not at higher temperatures. Humidity does generally not show a direct influence on viral stability. However, there may be an indirect influence by affecting chemical action on the virus and by increasing the inactivation rate by sunlight. No information has been provided in regard to temperature range at which CpGV is capable to proliferate. Dispersal of CpGV includes small animals and birds (their faeces are able to contain infective viruses), predators, wind blow of dry soil and rain splash at canopy edges. Knowledge of the importance of such mechanisms is scant.
Relationships to known plant, animal or human pathogens:	CpGV as well as all other baculoviruses are not related to any known plant, animal (other than arthropods) or human pathogen.
Genetic stability:	As judged from restriction endonuclease analyses comparing the same CpGV isolate propagated in different institutions over several years CpGV is genetically stable. Furthermore, the isolates used in different formulations for several years did not change genetically compared to the originally described Mexican isolate CpGV-M. In very rare cases, CpGV may acquire genes and transposable elements from its host. Horizontal gene transfer has been occurring frequently within baculoviruses and indicates a role for baculoviruses as vectors of horizontal DNA transfer between insects. However, these mutants are considered to be out-competed by the wildtype CpGV and do not establish in a mixture. Host DNA inserted into the viral genome is evidently not maintained in any viral population after several successive infection cycles. Thus, although it cannot be excluded that a single virus may contain host DNA sequences, the recorded stability of the CpGV genome provides evidence that these mutants are extremely seldom and do not establish during the production process.
Information on the production of relevant metabolites (especially toxins):	Viruses have no metabolism of their own and are therefore not able to produce secondary metabolites.
Resistance/ sensitivity to antibiotics / anti-microbial agents used in human or veterinary medicine:	Not applicable as viruses are not metabolically active and thus, do not produce antimicrobial substances. Furthermore, viruses are not sensitive to antibiotics or other antimicrobial drugs and, accordingly, cannot become resistant to these substances or spread resistance.

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Summary of uses supported by available data (Regulation (EU) N° 283/2013, Annex Part B, point 3)

GAP rev. 1, date: 2021-January-15

Active Substance:
CARPOVIRUSINE *Cydia pomonella* Granulovirus (CpGV, Mexican isolate)
MADEX *Cydia pomonella* Granulovirus (CpGV, Mexican isolate)
MADEX TWIN *Cydia pomonella* Granulovirus (CpGV-V22)
VIRGO *Cydia pomonella* Granulovirus (CpGV, Mexican isolate)

Crop and/or situation (a)	**Member State or Country**	**Product name**	**F G or I** (b)	**Pests or Group of pests controlled** (c)	**Preparation**		**Application**				**Application rate per treatment**			**PHI (days)** (m)	**Remarks**
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	kg a.s /hL min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		

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Germany	**October 2020**	***Cydia pomonella* GV**

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	kg a.s /hL min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		
Pome fruit (apple, pear, quince, nashi) Stone fruit (peach, apricot) Walnut	*EU*	CARPOVIRUSINE	*F*	Codling moth (*Cydia pomonella*) Oriental fruit moth (*Grapholitha molesta*)	*SC*	1×10^{13} GV/L product	Foliar spray (tractor drawn)	BBCH 71-89	*10*	*10 days*	1 l product / ha / application	*1000*	1×10^{13} GV/ha	*1*	The 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)
Pome fruit (apple, pear, quince, nashi) Stone fruit (peach, apricot) Walnut	*EU*	CARPOVIRUSINE	*Fn*	Codling moth (*Cydia pomonella*) Oriental fruit moth (*Grapholitha molesta*)	*SC*	1×10^{13} GV/L product	Foliar spray (Knapsack sprayer)	BBCH 71-89	*10*	*10 days*	1 l product / ha / application	*1000*	1×10^{13} GV/ha	*1*	Home gardening; Max. tree height: 2 m; The 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)
Pome fruit (apple, pear, quince, nashi, *Mespilus*) Walnut	EU	*MADEX*	F	Codling moth (*Cydia pomonella*)	*SC*	3×10^{13} GV/L product	Foliar spray (tractor drawn)	Before first larvae hatch from eggs*[1] (BBCH 71-89)	*10*	*6 days*[*2]	0.1 l product / ha / application	*400-1200*	0.3×10^{13} GV/ha	-	The application rate of 0.1 L/ha corresponds to 0.0875 L/ha LWA (leaf wall area)
Pome fruit (apple, pear, quince,	EU	*MADEX*	Fn	Codling moth (*Cydia pomonella*)	*SC*	3×10^{13} GV/L product	Foliar spray (Knapsack spray	Before first larvae hatch from eggs*[1] (BBCH 71-89)	*10*	*6 days*[*2]	0.1 l product / ha / application	*400-1200*	0.3×10^{13} GV/ha	-	Home gardening Max. tree height: 2 m The application rate of 0.1 L/ha corresponds to 0.0875 L/ha LWA

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Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	kg a.s /hL min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		
nashi) Walnut							er)								(leaf wall area)
Stone fruit (apricot, peach, nectarine, almond, plum)	*EU*	*MADEX TWIN*	F	Oriental fruit moth (*Grapholita molesta*)	*SC*	3 × 10^{13} GV/L	Foliar spray (tractor drawn)	Before first larvae hatch from eggs (BBCH 71-89)	*12*	*6-8*2*	0.1 l product / ha / application*3	*800*	0.3 × 10^{13} GV/ha	-	
Stone fruit (apricot, peach, nectarine, almond, plum)	*EU*	*MADEX TWIN*	F n	Oriental fruit moth (*Grapholita molesta*)	*SC*	3 × 10^{13} GV/L	Foliar spray (Knapsack sprayer)	Before first larvae hatch from eggs (BBCH 71-89)	*12*	*6-8*2*	0.1 l product / ha / application*3	*800*	0.3 × 10^{13} GV/ha	-	Home gardening
Pome fruit (apple, pear, quince, nashi) Walnut	*EU*	*VIRGO*	F	Codling moth (*Cydia pomonella*)	*SC*	2 × 10^{13} GV/L product	Foliar spray (tractor drawn)	BBCH 71-87	*6*	*7*	0.75 l product / ha / application	*1500-1700*4*	1.5 × 10^{13} GV/ha	*3*	Minimum dose rate: 0.5 L/ha; The application rate of 0.75 L/ha corresponds to 0.656 L/ha LWA (leaf wall area).

*1 First treatment 85 degree days after the first warm evening with flight activity. Zero point of development of the codling moth is 10°C.
*2 sunny days, counting 2 partially sunny days as 1 day
*3 This application rate of 0.1 L/ha corresponds to 0.0875 L/ha LWA (leaf wall area).
*4 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 very 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.

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)	(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)	
(c) *e.g.* biting and sucking insects, soil born insects, foliar fungi, weeds	

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(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	(j) Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of applications possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

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Germany	**October 2020**	***Cydia pomonella* GV**

Classification and proposed labelling (Symbol, Indication of danger, Risk phrases, Safety phrases)

with regard to physical/chemical data:	Not required
with regard to toxicological data:	Not applicable to viruses. Commercial products should be labelled as follows: 'Micro-organisms may have the potential to provoke sensitising reactions'.
with regard to fate and behaviour:	No classification required.
with regard to ecotoxicological data:	No classification required.

Methods of analysis (Regulation (EU) N° 283/2013, Annex Part B, point 4 and Regulation (EU) N° 284/2013, Annex Part B, point 5)

Analytical methods for the microorganism (MA 4.1 & MP 5.1)

Manufactured microorganism (principle of method):	Isolate identification by Restriction Fragment Analysis (RFLP) or single nucleotide polymorphism (SNP) Determination of the active ingredient by a standard bioassay with the target pest.
Impurities and contaminating microorganisms in manufactured material (principle of method):	Standard microbiological methods (EN ISO) for microbial contaminant screening including *B. cereus* according to SANCO/12116/2012-rev.0
Microbial Pest Control Product (principle of method):	See above, methods for the microorganism

Analytical methods for residues (viable and non-viable) in exposed compartments and organisms (MA 4.2 & MP 5.2)

of the active microorganism (principle of method):	Methods are not required.
of relevant metabolites (principle of method):	Methods are not required.

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Impact on Human and Animal Health (Regulation (EU) N° 283/2013, Annex Part B, point 5 and Regulation (EU) N° 284/2013, Annex Part B, point 7)

Medical data: (including medical surveillance on manufacturing plant personnel) (MA 5.1.1))	No evidence of adverse effects on humans, not related to human or animal pathogens
Sensitisation: (MA 5.2.1 & MP 7.2.3)	No evidence for the virus itself, formulations may be sensitising or not, due to larval proteins from virus propagation or co-formulants
Acute oral infectivity, toxicity and pathogenicity: (MA 5.2.2.1 & MP 7.1.1)	No evidence of adverse effects, $LD_{50} > 1.015 \times 10^8$ granules/animal (rat)
Acute intratracheal/inhalation infectivity, toxicity and pathogenicity: (MA 5.2.2.2 & MP 7.1.2)	No evidence of adverse effects, $LC_{50} > 2 \times 10^{13}$ granules/L (rat, inhalation, product study)
Acute intravenous/intraperitonial infectivity: (MA 5.2.2.3)	No evidence of adverse effects, $LD_{50} > 1.015 \times 10^7$ granules/animal (rat, i.p.)
Genotoxicity: (MA 5.2.3)	Negative in studies of limited scientific value, not likely because of general knowledge on baculoviruses
Cell culture study: (MA 5.2.4)	CpGV penetrated into human W138 cells but did not replicate there, no transcription of viral genes
Information on short-term toxicity and pathogenicity: (MA 5.2.5)	No reliable data, not necessary
Dermal toxicity: (MP 7.1.3)	No data, not necessary
Specific toxicity, pathogenicity and infectivity: (MA 5.3)	No reliable data, not necessary
Genotoxicity – *in vivo* studies in germ cells: (MA 5.5)	No data, not necessary

Reference values

AOEL:	Not applicable to viruses
ADI:	Not applicable to viruses
ARfD:	Not applicable to viruses

Exposure (operator, workers, bystander, consumer): (MA 6.1 & MP 7.3, 8.0)	No health risk expected for operator, worker, bystander or residents for the intended uses. PPE is required for the operator with respect to the sensitising potential of micro-organisms.

Residues (Regulation (EU) N° 283/2013, Annex Part B, point 6 and Regulation (EU) N° 284/2013, Annex Part B, point 8)

Viable residues:	No risk for the consumer is expected from the micro-organism itself i.e. it is not pathogenic. Under considera-tion of a limit level of 10^7 CFU of *Bacillus cereus* per g or mL, a risk to consumers could not be identified.
Non-viable residues:	Non-viable residues (toxic metabolites or degradation products) do not occur.

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Fate and Behaviour in the Environment (Regulation (EU) N° 283/2013, Annex Part B, point 7 and Regulation (EU) N° 284/2013, Annex Part B, point 9)

Persistence and multiplication (competitiveness) in soil, water and air:	*Cydia pomonella* Granulovirus (CpGV) belongs to the group of baculoviruses. Baculoviruses are ubiquitous in the environment, their prevalence depending on the frequency of occurrence of their arthropod hosts. Granuloviruses have to be considered as persistent in soil, as they are protected from UV-light in deeper soil layers. Multiplication can restart again if the permissive host appears. Granuloviruses precipitate quickly in an aquatic system at similar rates as soil particles. Transport into the sediment phase is likely. Activity in sediment remaining for a length of time similarly as in soil cannot be excluded. The virus is inactivated by sun light. A half-life of 52 hours was determined. Occlusion bodies of granuloviruses can be considered as suspended solid particles that are non-volatile. Therefore a distribution of CpGV via air can be excluded.
Mobility:	Granuloviruses are able to leach through a column of soil. Results of a field lysimeter experiment conducted 1987 Germany indicate an acceptable low risk of reaching deeper soil layers and therefore the groundwater. The good retention of baculoviruses by soil is probably attributed to the particular protein envelope of the virus particles consisting of granulin.

Effects on non-target organisms (Regulation (EU) N° 283/2013, Annex Part B, point 8 and Regulation (EU) N° 284/2013, Annex Part B, point 10)

Effects on birds (MA 8.1 & MP 10.1)

Application rate (kg MPCA/ha)	Test substance	Crop	Category (*e.g.* insectivorous bird) and species	Time-scale	Toxicity, infectivity and pathogenicity (endpoint, value or other description of effects)
max. total rate per crop and season: 1×10^{14} GV/ha (overall worst-case)	Carpo-virusine	Pome fruit Stone fruit Walnut	Test species: Northern bobwhite *Colinus virginianus*	30 days	NOEL and LD50 > 10,000 mg/kg bw/day, corresponding to 10^{11} granules/kg bw (5 days dosing period; resultant total dosage was 50,000 mg/kg over 5 days); No signs of toxicity, infectivity and pathogenicity.

Effects on mammals

Application rate (kg MPCA/ha)	Test substance	Crop	Category (*e.g.* herbivorous mammal) and species	Time-scale	Toxicity, infectivity and pathogenicity (endpoint, value or other description of effects)
max. total rate per crop and season:	Carpovirus ine	Pome fruit Stone fruit Walnut	Test species: Rat (Sprague-Dawley)	14 days (Post exposure	LD_{50} > 5,000 mg/kg bw, corresponding to > 4.9×10^{10} GV/kg bw;

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1×10^{14} GV/ha (overall worst-case)				observation period)	No signs of toxicity, infectivity or pathogenicity.

Effects on other terrestrial vertebrates

Application rate (kg MPCA/ha)	Test substance	Crop	Group (*e.g.* amphibian) and species	Time-scale	Toxicity, infectivity and pathogenicity (endpoint, value or other description of effects)
No information provided.					

Effects on aquatic organisms (MA 8.2 & 10.2)

Group	Test substance	Time-scale	Toxicity, infectivity and pathogenicity (endpoint, value or other description of effects)
Laboratory tests			
Fish species (specify):			
Danio rerio	Carpovirusine	96 hours	LC_{50} > 250 mg/L, corresponding to 1.0×10^9 GV/L; No signs of toxicity/infection/pathogenicity
Oncorhynchus mykiss	Madex (= Granulosevirus CpGV SC)	96 hours	LC_{50} > 150 mg/L, corresponding to 2.0×10^9 GV/L; No signs of toxicity/infection/pathogenicity
Oncorhynchus mykiss	Virgo	96 hours	LC_{50} > 100 mg/L, corresponding to 1.61×10^9 GV/L; No signs of toxicity/infection/pathogenicity
Invertebrate species: (specify)			
Daphnia magna	Carpovirusine	48 hours	EC_{50} > 250 mg/L, corresponding to 1.0×10^9 GV/L; No signs of toxicity/infection/pathogenicity
Daphnia magna	Madex (= Granulosevirus CpGV SC)	48 hours	EC_{50} > 100 mg/L, corresponding to > 2.0×10^9 GV/L; No signs of toxicity/infection/pathogenicity
Daphnia magna	Virgo	48 hours	EC_{50} > 100 mg/L, corresponding to 1.61×10^9 GV/L; No signs of toxicity/infection/pathogenicity

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Effects on algae: (species, growth, growth rate, capacity to recover) (MA 8.2.3 & MP 10.2)	unicellular green alga (*Pseudokirchneriella subcapitata*); Test substance: Carpovirusine; EC_{50}> 100 mg/L, corresponding to 9.8 × 10^8 GV/L (= 1 × 10^9 GV/L); no signs of toxicity, infectivity or pathogenicity; green alga (*Scenedesmus subspicatus = Desmodesmus subspicatus*); Test substance Madex (= Granulosevirus CpGV SC); EC_{50}> 100 mg/L, corresponding to 1.0 × 10^9 GV/L; no signs of toxicity, infectivity or pathogenicity unicellular green alga (*Pseudokirchneriella subcapitata*); Test substance: Virgo; EC_{50}> 100 mg/L, corresponding to 1.61 × 10^9 GV/L; no signs of toxicity, infectivity and pathogenicity
Effects on aquatic plants (species, growth, growth rate, capacity to recover)(MA 8.2.4 & MP 10.2)	gibbous duckweed (*Lemna gibba*); Test substance: Madex (= Granulosevirus CpGV SC); EC_{50}> 100 mg/L, corresponding to 1.0 × 10^9 GV/L; no signs of toxicity, infectivity or pathogenicity common duckweed (*Lemna minor*); Test substance: Virgo; EC50> 100 mg/L, corresponding to 1.61 × 10^9 GV/L; no signs of toxicity, infectivity or pathogenicity

Effects on bees (Regulation (EU) N° 283/2013, Annex Part A, point 8.3.1 and Regulation (EU) N° 284/2013 Annex Part A, point 10.3.1)

Species	Test substance	Time scale/type of endpoint	End point	Toxicity
Apis mellifera L.	*Carpovirusine*	acute	oral toxicity 48h (LD_{50})	> 1.63 x 10^6 µg CpGV/bee (> 108.4 µg product/bee)
			contact toxicity 48h (LD_{50})	> 1.63 x 10^6 µg CpGV/bee (> 100 µg product/bee)
	Virgo	acute	oral toxicity 72h (LD_{50})	> 1.63 x 10^6 µg CpGV/bee (> 100 µg product/bee)
			contact toxicity 72h (LD_{50})	> 1.63 x 10^6 µg CpGV/bee (> 100 µg product/bee)
	*Madex** *Madex Twin**	acute	oral toxicity 48h (LD_{50})	> 3.5 x 10^7 µg CpGV/bee
			contact toxicity 48h (LD_{50})	> 4.4 x 10^7 µg CpGV/bee

CpGV: *Cydia pomonella* Granulovirus

* tested as Granupom. 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 ganules/L. Therefore their comparability is considered as sufficient.

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Potential for accumulative toxicity: no data	
Infectiveness and pathogenicity:	To investigate the infectiveness and pathogenicity several laboratory studies have been generated by a literature research and were evaluated. No toxic or pathogenic effects were observed.
Further information*:	The reliable information from the literatures regarding the impact on honey bee colonies was tested in tow field studies (Cantwell 1966; Knox 1970) and one laboratory study (Gröner 1978). The results do not indicate any harmful effects on colony development or bee mortality. No signs of an impact of brood development in bumble bees colonies could be detected in another study (Mommaerts, V. et al., 2009). It was reported that the host range of granuloviruses appears to be even narrow and mostly restricted to a single species. Furthermore, the high host specificity of CpGV to only a few species of Tortricidae family (Lepidoperta) was also reported (for more information refer to Volume 3 – B.2 Biological properties). Altogether, the risk for bee larvae or, in general, for the bee brood could be assumed as negligible. Information on data already evaluated are re-evaluated and reported.

* A new study on bumble bees with the product Granupom (active substance: *Cydia pomonella* granulovirus, concentration 2.2 × 10^{13} CFU/g) was submitted (B.9.3.1/1 (Mommaerts et al, 2009). However, as the study was considered only as supportive information no summary is listed here.

Risk assessment

The recommended use pattern for *Cydia pomonella* granulovirus (CpGV) includes application in orchards (pome and stone fruits) and walnuts at a maximum application rat of up to 0.75 L VIRGO/ha (1.5 x 10^{13} CpGV/ha).
As CpGV is a microorganism, calculation of hazard quotients (HQ) according to EPPO Environmental Risk Assessment Scheme does not seem to be appropriate.

Effects on terrestrial arthropods other than bees (MA 8.4 & MP 10.4)

Species	Stage	Test Substance	Dose (kg MPCA/ha)	Toxicity, infectivity and pathogenicity (endpoint, value or other description of effects)
Laboratory Tests				
Hippodamia convergens	adult	Carpovirusine	55 - 550 - 5500 ppm treatment group (corresponding to 5.5 × 10^{8}, 5.5 × 10^{9} and 5.5 × 10^{10} GV/g diet);	30 day-LC_{50} > 5500 ppm; 30 day-LC_{50} > 5500 ppm; 30 day-NOEC ≥ 5500 ppm (corresponding to 5.5 x 10^{10} GV/g food); no signs of toxicity/infectivity/pathogenicity

List of end points

Rapporteur Member State	Month and year	Microbial or Viral Agent (Name)
Germany	**October 2020**	***Cydia pomonella* GV**

			administered by honey	
Chrysoperla carnea	larva	Carpovirusine	55 - 550 - 5500 ppm treatment group (corresponding to 5.5×10^8, 5.5×10^9 and 5.5×10^{10} GV/g diet); administered in a moth egg diet	10 day-LC_{50} > 5500 ppm; 10 day-LC_{50} > 5500 ppm; 10 day-NOEC ≥ 5500 ppm (corresponding to 5.5 x 10^{10} GV/g food); no signs of toxicity/infectivity/pathogenicity
Aphidius rhopalosiphi	adult	Carpovirusine	37 – 111 – 333 – 1000 – 3000 mL/ha ; extended Laboratory Study using treated barley seedlings/food	48 hour-LR_{50} > 3000 mL/ha; 48 hour-ER_{50} > 3000 mL/ha; no signs of toxicity/infectivity/pathogenicity
Typhlodromus pyri	proto-nymphs	Carpovirusine	37 – 111 – 333 – 1000 – 3000 mL/ha ; extended Laboratory Study; applied on leaf surfaces/food	7 day-LR_{50} > 3000 mL/ha; 7 day-ER_{50} > 3000 mL/ha; no signs of toxicity/infectivity/pathogenicity
Aphidius rhopalosiphi	proto-nymphs	Madex (= Granulose-virus CpGV SC)	360 mL/ha (Limit test); exposure to treated glass plates	48 hour-LR_{50} > 360 mL/ha; 48 hour-ER_{50} > 360 mL/ha; (corresponding to 7.92×10^{12} GV/ha); no signs of toxicity/infectivity/pathogenicity; Given the specific mode of action, exposure scenario via treated glass plates (without treated food) not suitable to detect possible effects of CpGV on *Aphidius rhopalosiphi*
Typhlodromus pyri	proto-nymphs	Madex (= Granulose-virus CpGV SC)	360 mL/ha (Limit test); exposure to treated glass plates	7 day-LR_{50} > 360 mL/ha; 7 day-ER_{50} > 360 mL/ha; (corresponding to 7.92×10^{12} GV/ha); no signs of toxicity/infectivity/pathogenicity; Given the specific mode of action, exposure scenario via treated glass plates (without treated food) not suitable to detect possible effects of CpGV on *Typhlodromus pyri*
Poecilus cupreus	proton-ymphs	Madex (= Granulose-virus CpGV SC)	360 mL/ha (Limit test); exposure to treated quartz sand/food	14 day-LR_{50} > 450 mL/ha; 14 day-ER_{50} > 450 mL/ha (corresponding to 9.9×10^{12} GV/ha); no signs of toxicity/infectivity/pathogenicity
Aphidius rhopalosiphi	proto-nymphs	Virgo	1725 mL/ha (Limit test);	48 hour-LR_{50} > 1725 mL/ha; 48 hour-ER_{50} > 1725 mL/ha

			exposure to treated glass plates	(corresponding to 3.45×10^{13} GV/ha); no signs of toxicity/infectivity/pathogenicity; Given the specific mode of action, exposure scenario via treated glass plates (without treated food) not suitable to detect possible effects of CpGV on *Aphidius rhopalosiphi*
Typhlodromus pyri	proto-nymphs	Virgo	1725 mL/ha (Limit test); exposure to treated glass plates	7 day-LR_{50} > 1725 mL/ha; 7 day-ER_{50} > 1725 mL/ha (corresponding to 3.45×10^{13} GV/ha); no signs of toxicity/infectivity/pathogenicity; Given the specific mode of action, exposure scenario via treated glass plates (without treated food) not suitable to detect possible effects of CpGV on *Typhlodromus pyri*

Effects on other terrestrial invertebrates (MA 8.5 & MP 10.5)

Toxicity, infectivity and pathogenicity: (endpoint, value or other description of effects)	Test substance Carpovirusine: Acute study with *Eisenia fetida*; 14 day-LC_{50}> 1000 mg/kg soil dw; no signs of toxicity, infectivity and pathogenicity; Reproduction study with *Eisenia fetida*: 56 day-NOEC ≥ 1000 mg/kg soil dw; no signs of toxicity, infectivity or pathogenicity Test substance Madex (= CpGV SC): Acute study with *Eisenia fetida*; 14 day-LC_{50}> 1000 mg/kg soil dw, corresponding to 1.67×10^{10} GV/kg soil dw; no signs of toxicity, infectivity or pathogenicity Test substance Virgo: Acute study with *Eisenia foetida*; 14 day-LC_{50}> 1000 mg/kg soil dw, corresponding to 1.61×10^{10} GV/kg soil dw; no signs of toxicity, infectivity or pathogenicity
Further information:	Literature search did not indicate any adverse effects on earthworms associated with the use of baculoviruses.

Effects on soil microorganisms (MA 8.6 & MP 10.6)

All formulations tested (Carpovirusine, Madex, Virgo) had no negative impact on nitrogen transformation and soil respiration. In conclusion, CpGV represents no hazard to soil microorganisms.

Additional studies (MA 8.7 & MP 10.7)

No additional studies have been conducted.