Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the Evaluation of the New Active CYDIA POMONELLA GRANULOSIS VIRUS STRAIN V22 in the Product GRANDEX BIOLOGICAL INSECTICIDE

APVMA Product Number P69674

JULY 2015

ISSN: 1443-1335
ISBN: 978-1-922188-93-9

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This publication is available from the APVMA website: www.apvma.gov.au.

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing, Office of Chemical Safety (OCS), Department of Environment (DoE), and State Departments of Primary Industries.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of Public Release Summaries for products containing new active constituents.

The information and technical data required by the APVMA to assess the safety of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined in the APVMA's publications and Regulatory Guidelines.

This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice it received from its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

About this document

This is a Public Release Summary.

It indicates that the Australian Pesticides and Veterinary Medicines Authority (APVMA) is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested stakeholders on the information contained within this document.

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of GRANDEX BIOLOGICAL INSECTICIDE should be granted. Submissions should relate only to matters that the APVMA is required, by legislation, to take into account in deciding whether to grant the application. These matters include aspects of public health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop or animal safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on 11 August 2015 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address (if available)
- the date you made the submission.

All personal information, and confidential information judged by the APVMA to be *confidential commercial information (CCI)*[1] contained in submissions will be treated confidentially.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the grounds for registration should be addressed in writing to:

Case Management and Administration Unit
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Phone: +61 2 6210 4701

[1] A full definition of 'confidential commercial information' is contained in the Agvet Code

Fax: +61 2 6210 4741

Email: enquiries@apvma.gov.au

Further information

Further information can be obtained via the contact details provided above.

Copies of evaluation report covering environmental aspects are available from the APVMA on request.

Further information on public release summaries can be found on the APVMA website: www.apvma.gov.au

1 INTRODUCTION

1.1 Purpose of Application

Andermatt Biocontrol AG has applied to the APVMA for registration of the new product GRANDEX BIOLOGICAL INSECTICIDE containing the new active constituent Cydia Pomonella Granulosis Virus Strain V22 in the form of a suspension concentrate (SC) formulation.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of GRANDEX BIOLOGICAL INSECTICIDE containing the new active constituent Cydia Pomonella Granulosis Virus Strain V22 (CpGV- V22).

1.2 Mode of action

The baculovirus CpGV-V22 acts as a biological stomach insecticide against larvae of codling moth (*Cydia pomonella*) and oriental fruit moth *(Grapholita molesta*).

Ingestion by susceptible larvae leads to the granules being dissolved in the midgut and free virions being released that invade midgut cells by fusion with the microvilli. As a polyorganotropic disease, other tissues are also invaded, eventually resulting in death of the larvae before pupation can occur. The body of the insect then liquefies.

While the virus is released into the environment once the host larva has liquefied and could infect other larvae, the rapid inactivation of the virus by sunlight results in the need for re-application of the product to ensure subsequent hatching larvae are controlled.

1.3 Product claim and use pattern

GRANDEX BIOLOGICAL INSECTICIDE (the product) is intend for the control of codling moth and oriental fruit moth in pome and stone fruits. The product is intended to be used in all states.

1.4 Overseas registration

GRANDEX is registered as Madex Twin in the EU and MADEX HP in the US.

2 CHEMISTRY AND MANUFACTURE

The active constituent Cydia pomonella granulosis virus strain V22 has the following properties:

COMMON NAME (ISO):	Cydia Pomonella Granulosis Virus Strain V22 (CpGV-V22)
CHEMICAL NAME:	N/A
PRODUCT NAME:	Grandex Biological Insecticide
CAS REGISTRY NUMBER:	N/A
EMPIRICAL FORMULA:	N/A
MOLECULAR WEIGHT:	N/A
PHYSICAL FORM:	Grey-brown liquid (200C)
COLOUR:	Grey-brown
DENSITY:	1100 kg/m3
STRUCTURAL FORMULA:	N/A

The product Grandex Biological Insecticide will be manufactured overseas and imported into Australia in 100 mL to 20 L polyethylene terephthalate (PET) or high density polyethylene (HDPE) containers.

Physical and Chemical Properties of the Product

PROPERTY	RESULTS
Appearance	Grey brown liquid with typical odour
Relative Density	1.16
Pourability	Residue: 1.05% Rinsed Residue: 0.16%
Spontaneity of Dispersion	89–105%
Suspensibility	86–93%
Persistent Foam	0 mL
Foaming of Suspension Concentrates	0 mL
Kinematic Viscosity	39.0 mm^2/s @ 20°C 25.0 mm^2/s @ 30°C 17.1 mm^2/s @ 40°C

PROPERTY	RESULTS
Surface Tension	39.9 mN/m @ 20°C
pH	6.4 (1% w/v aqueous dilution)
Sieve Analysis	1.1% 140µm 1.2% 125µm 1.6% 100µm 2.5% 75µm

3 TOXICOLOGICAL ASSESSMENT

The Office of Chemical Safety (OCS) in the Department of Health has advised that the proposed product Grandex Biological Insecticide containing a new strain of the Cydia Pomonella Granulosis Virus (*Cp*GV-V22) is considered to have a similar public health risk profile to that of the currently approved strain (*Cp*GV-M) present in the registered reference product Madex Biological Insecticide (63025). On this basis OCS has recommended that the proposed product would not be likely to have an effect that is harmful to human beings and that the existing First Aid Instructions and Safety Directions are adequate.

4 RESIDUES ASSESSMENT

An assessment of the application for Grandex Biological Insecticide was undertaken by the APVMA. The APVMA has determined that the proposed product Grandex Biological Insecticide containing a new strain of the Cydia Pomonella Granulosis Virus (*Cp*GV-V22) for use on pome fruit and stone fruit is covered in the MRL Standard by the current Table 5 entry for Cydia Pomonella Granulosis Virus as an insecticide. Table 5 includes *Uses of substances where MRLs are not necessary*.

5 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

As for *Toxicological Assessment* above the Office of Chemical Safety (OCS) in the Department of Health has advised that the proposed product Grandex Biological Insecticide containing a new strain of the Cydia Pomonella Granulosis Virus (*Cp*GV-V22) is considered to have a similar public health risk profile to that of the currently approved strain (*Cp*GV-M) present in the registered reference product Madex Biological Insecticide (63025). On this basis OCS has recommended that the proposed product would not be likely to have an effect that is harmful to human beings and that the existing First Aid Instructions and Safety Directions are adequate.

6 ENVIRONMENTAL ASSESSMENT

The active constituent *Cydia pomonella* GV strain V22 (*Cp*GV-V22) is a naturally occurring insect virus that is isolated from codling moth. C*p*GV-V22 was considered to be closely similar to the active constituent *Cp*GV-M that is currently used in the nominated reference product Madex Biological Insecticide (product number 63025). Grandex and Madex Biological Insecticides are identical in their physical, chemical and technical properties; the only variation is that the virus isolate differs.

Due to small genetic difference as shown by REN (restriction-endonuclease), phylogenic analysis, and genome sequencing it was concluded that *Cp*GV-V22 is almost identical to the active constituent *Cp*GV- M.

C*p*GVs are granuloviruses (GVs) which is one of two genera taxonomically classified in the family Baculoviridae. Baculoviruses can persist in the environment from hours to days to years especially in the soil where they are immobile. The persistence is highly dependent on UV radiation and other factors such as temperature, humidity and precipitation. The limited lifetime of baculovirus insecticides in the environment, to a great extent caused by their sensitivity for sunlight (UV).

C*p*GVs are not known to be active to organisms other than the moth larvae of the family Tortricidae. Available data indicate that C*p*GVs are classified as harmless to predators or parasites, such as a predatory mite *(Typhlodromus pyri)*, a ground beetle *(Poecilus cupreus)*, other predator insects (i.e. fillips, clerids, pentatomids and minds), and parasitic wasps *(Aphidius rhopalosiphi*). In addition, C*p*GV treatment did not

have any effect on San Jose scale *(Aspidiotus perniciosus),* mealybugs or woolly aphid *(Eriosma lanigerum)*. As a result, it was concluded that the use of Grandex Biological Insecticide will not cause greater risk to non-target organisms than that posed by the nominated reference product, Madex Biological Insecticide.

7 EFFICACY AND SAFETY ASSESSMENT

The efficacy of Grandex Biological Insecticide was evaluated in three bioefficacy trials examining the control of Codling moth in pome fruit orchards and four bioefficacy trials for the control of Oriental fruit moth (OFM) in stone fruit orchards, covering a range of pest intensities.

For the pome fruit trials, Madex Biological Insecticide was used as a reference product, and in one case another industry standard product was included, Sumitomo Samurai Systemic Insecticide (clothianidin). For the stone fruit trials, efficacy was compared to the industry standard Calypso 480 SC Insecticide (thiacloprid). All the studies were conducted using replicated small plots (evaluating 1–2 trees per plot) on commercial orchards. Foliar application was by power operated hand lance, with dilute spraying to runoff. Efficacy was evaluated by inspection for damage to fallen fruit and fruit on the trees at 1–3 occasions during the season as well as at harvest, plus inspection for tip damage from OFM.

The outcome of the bioefficacy trials supports the label claims for similar efficacy to the reference product Madex Biological Insecticide for the control of Codling moth in pome fruit orchards. The outcome of the bioefficacy trials also supports the label claim for efficacy against OFM in stone fruits. However, for both pests, particularly under high pest pressure additional control measures may be needed to achieve adequate control. The draft label carries appropriate advice to assist users in achieving satisfactory control of both codling moth and OFM.

The crop safety of Grandex Biological Insecticide in pome and stone fruits was evaluated as part of the bioefficacy trials. These studies confirmed crop safety to pome and stone fruit under the proposed use regimes.

The label directions for Grandex closely follow those for the existing Madex label, with the addition of instructions dealing with OFM.

8 LABELLING REQUIREMENTS

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Grandex®
Biological Insecticide

ACTIVE CONSTITUENT: $3x10^{13}$ granula /L *CYDIA POMONELLA* GRANULOSIS VIRUS

A biological agent to control codling moth and oriental fruit moth in pome and stone fruits

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE.

CONTENTS: [100 mL – 20L]

APVMA APPROVAL No: xxxx/xxxxx

Organic Crop Protectants
Unit 1/61, Turrella St, TURRELLA NSW 2205

BACK PANEL

STORAGE AND DISPOSAL:
Keep out of reach of children. Store in the closed, original container out of direct sunlight. The product can be stored for short periods (14 days) at room temperature. For long term storage (2 years) keep refrigerated at less than 5°C.
Triple rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemical on site. If not recycling, break, crush or puncture and deliver empty packaging to an approved waste management facility. DO NOT burn empty containers or product.

SAFETY DIRECTIONS:
May irritate the eyes and skin. Repeated exposure may cause allergic disorders. Avoid contact with the eyes and skin. When opening the container and preparing the spray, wear elbow-length chemical-resistant gloves and goggles or safety glasses. Wash hands after use.

FIRST AID:
If poisoning occurs, contact a doctor or Poisons information Centre (telephone 13 11 26).

MATERIAL SAFETY DATA SHEET:
Additional information is listed in the Material Safety Data Sheet available from the supplier.

Batch No:
DOM:
Expiry date: 2 years from DOM when stored at less than 5°C.

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Grandex®
Biological Insecticide

ACTIVE CONSTITUENT: $3x10^{13}$ granula /L *CYDIA POMONELLA* GRANULOSIS VIRUS

A biological agent to control codling moth and oriental fruit moth in pome and stone fruits

IMPORTANT: READ THIS LEAFLET BEFORE USE.

APVMA APPROVAL No: xxxx/xxxx

® Grandex is a Registered Trademark of Andermatt Biocontrol, Switzerland

Organic Crop Protectants
Unit 1/61, Turrella St, TURRELLA NSW 2205

DIRECTIONS FOR USE

SPRAY DRIFT RESTRAINTS

DO NOT apply within 48 hours of expected precipitation or during heavy rainfall. **DO NOT** disturb soil for 48 hours after application.
ONLY APPLY with orchard application spray equipment.
DO NOT apply when wind speed is less than 3 or more than 20 km per hour as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.
Users of this product **MUST make an accurate written record** of the details of each spray application within 24 hours following application and KEEP this record for a minimum of 2 years. The spray application details that must be recorded are: (1) date with start and finish times of application; (2) location address and paddock/s sprayed; (3) full name of this product; (4) amount of product used per hectare and number of hectares applied to; (5) crop/situation and weed/pest; (6)
wind speed and direction during application; (7) air temperature and relative humidity during application; (8) nozzle brand, type, spray angle, nozzle capacity and spray system pressure measured during application; (9) name and address of person applying this product.
(Additional record details may be required by the state or territory where this product is used.)
DO NOT apply when there are native forests, aquatic and wetland areas including aquacultural ponds or
surface streams and rivers downwind from the application area and within the mandatory nospray zone shown below.

MANDATORY NO-SPRAY ZONE

DO NOT apply when there are native forests, aquatic and wetland areas including aquacultural ponds or surface streams and rivers within 40 m downwind from the application area.

Crop	Pest	Rate (L/ha)	Critical Comments
Pome fruit	Codling moth (*Cydia pomonella*) Oriental fruit moth (*Grapholita molesta*)	7 mL / 100L (100 mL/ha)	Use 100 mL Grandex in 1500–2000 litres of water per hectare. High volumes will be required in older orchards with large trees to obtain proper coverage of fruit. Apply as a dilute spray to the point of runoff. Grandex mixes readily with water. Timing of applications is critical to ensure larvae are exposed to sufficient concentration of the virus. Make the first application from petal fall onwards when newly hatched codling moth and oriental fruit moth larvae are present in the orchard. This should be based on pheromone trap catches of codling moths in orchards. Larvae will be present within 4 weeks of moth catches. Alternatively, use the appropriate amount of 'degree days' for your area to determine egg hatch as recommended by your local advisor. Apply at 7 to 14 day intervals while codling moth larvae are present. Use the shorter interval during periods of high sunlight intensity (long sunny days). Most areas of Australia will have 3 or more

			generations per season and so it is important to monitor for each generation. For areas where there is considerable generational overlap, regular applications will be required for maximum effect.
Stone fruit	Oriental fruit moth (*Grapholita molesta*)		Use 100 mL Grandex in 1500–2000 litres of water per hectare. High volumes will be required in older orchards with large trees to obtain proper coverage of fruit. Apply as a dilute spray to the point of runoff. Grandex mixes readily with water. Timing of applications is critical to ensure larvae are exposed to sufficient concentration of the virus. Make the first application when newly hatched Oriental fruit moth larvae are present in the orchard. This should be based on pheromone trap catches of Oriental fruit moths in orchards. Apply at 7 to 14 day intervals while Oriental fruit moth larvae are present. Use the shorter interval during periods of high sunlight intensity (long sunny days).

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION

WITHHOLDING PERIOD: NOT REQUIRED WHEN USED AS DIRECTED.

GENERAL INSTRUCTIONS

Correct application of Grandex will result in high mortality of larvae in even high density populations. If used to treat all generations in consecutive seasons, especially over large areas, large reductions in Codling moth and Oriental fruit moth will be achieved. However, where heavy infestations of Codling moth or Oriental fruit moth are present in orchards, young larvae can still cause considerable damage on the surface of fruits before being killed by the virus.

Grandex should therefore be used as part of an integrated pest management strategy. Other compatible methods such as pheromone mating disruption dispensers can be used to complement the control achieved by applications of Grandex. Particularly when heavy infestations are present, it is important to use such measures to reduce the population to levels where damage can be better managed by Grandex.

The use of additional control measures is also important to minimise the risk of resistance to Grandex developing with repeated, ongoing use.

To assist in reducing migration of mated female moths into the treated area, it is highly advisable to clean up any accessible areas where refuges of untreated moths may be harbouring, e.g. fruit trees not receiving any pesticide treatment to control larvae, packing sheds or any areas with fruit that could contain Codling moth or Oriental fruit moth larvae.

MIXING

Grandex mixes readily with water for application.

COMPATIBILITY
Do not mix with pesticides that have a pH of less than 5.0 or greater than 8.5 in solution as the virus may be deactivated.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
DO NOT contaminate streams, rivers or waterways with this product or used containers.

STORAGE AND DISPOSAL
Keep out of reach of children. Store in the closed, original container out of direct sunlight. The product can be stored for short periods (14 days) at room temperature. For long term storage (2 years) keep refrigerated at less than 5°C.

Triple rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemical on site. If not recycling, break, crush or puncture and deliver empty packaging to an approved waste management facility. DO NOT burn empty containers or product.

SAFETY DIRECTIONS
May irritate the eyes and skin. Repeated exposure may cause allergic disorders. Avoid contact with the eyes and skin. When opening the container and preparing the spray, wear elbow-length chemical resistant gloves and goggles or safety glasses. Wash hands after use.

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DOM
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® Grandex is a Tradename of Andermatt Biocontrol, Switzerland.

APVMA Approval Number: xxxx/xxxx

ABBREVIATIONS

ac	active constituent
ai	active ingredient
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
EUP	End Use Product
Fo	original parent generation
g	gram
h	hour
ha	hectare
IPM	Integrated Pest Management
kg	kilogram
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NOEC/NOEL	No Observable Effect Concentration Level
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
s	second
REN	Restriction-endonuclease

SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGAC	Technical grade active constituent
µg	microgram
vmd	volume median diameter
WHP	Withholding Period

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	repels water
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octanol water partitioning co-efficient, synonym KOW
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons