Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new active d*uddingtonia flagrans* in the products BioWorma® and Livamol with BioWorma®

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CONTENTS

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 the Environment and Energy 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 on the APVMA website.

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 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 approval of the new active constituent *Duddingtonia flagrans* and registration of the products BioWorma and Livamol with BioWorma 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 13 March 2018 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
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

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

Further information

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

Further information on Public Release Summaries can be found on the APVMA website: www.apvma.gov.au

1 INTRODUCTION

1.1 Applicant

International Animal Health Products Pty Ltd.

1.2 Purpose of application

International Animal Health Products Pty Ltd has applied to the APVMA for approval of the new active constituent *Duddingtonia flagrans* strain IAH 1297 and for registration of two new products containing that constituent, BioWorma® containing not less than 500,000 chlamydospores per gram and Livamol® with BioWorma® containing not less than 30,000 chlamydospores per gram.

This publication provides a summary of the information reviewed and an outline of the regulatory considerations for the proposed registration of BioWorma and Livamol with BioWorma, and approval of the new active constituent, *Duddingtonia flagrans* strain IAH 1297.

1.3 Product claims and use pattern

BioWorma and Livamol with BioWorma are palatable feed supplements that contain the spores of *Duddingtonia flagrans,* a naturally occurring fungus commonly found in soil and pasture. It is a non-chemical biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals, which acts by substantially reducing the numbers of infective worm larvae (including chemical/anthelmintic multi-resistant larvae) emerging from manure onto pasture.

BioWorma and Livamol with BioWorma are provided as feed supplements and are dosed according to body weight with BioWorma to be fed at 6 g/100 kg bodyweight and Livamol with BioWorma to be fed at 100 g/100 kg bodyweight. Further details are provided on product labels as contained in Section 9.

1.4 Mode of action

Duddingtonia flagrans belongs to a group of nematophagous fungi that physically entrap nematodes by means of a specialised adhesive hyphal net. *D. flagrans* in the product consists largely of chlamydospores. When fed to animals, the thick-walled spores remain inert (having no effect within the host animal) and resist digestion, passing through into the manure. There they germinate and form trapping organs that capture, paralyse and consume emerging infective worm larvae (including multi-resistant larvae). The trap consists of a three dimensional network with sticky hyphae, where nematodes attach. This structure excludes effects on the majority of soil organisms other than nematodes. The crucial re-infestation stage of the parasites' life cycle is interrupted, reducing the amount of reinfection from contaminated pasture. This in turn reduces the number of nematodes able to migrate to herbage and re-infect the grazing animals (EFSA 2006).

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

Duddingtonia flagrans strain IAH 1297 is a nematophagous fungus, used as a biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals. It is a native non-GMO organism isolated from the Australian environment by CSIRO.

The active constituent is identified as below:

COMMON NAME:	*Duddingtonia flagrans* strain IAH 1297
SPECIES NAME:	*Duddingtonia flagrans*
STRAIN NAME:	IAH 1297
GENUS NAME:	*Duddingtonia*
FAMILY NAME:	*Orbilliaceae*
KINGDOM:	Fungi

The identity of the isolate, as well as for confirming the identity of batches of product and of environmental samples following use of the biocontrol agent, of the Duddingtonia flagrans strain IAH 1297 is confirmed by PCR based on polymorphisms unique to the strain.

Scanning electron micrographs of the chlamydospores of *Duddingtonia flagrans* strain IAH 1297 demonstrate a characteristic size between 19 and 24 µm.

The APVMA has evaluated the chemistry aspects of *Duddingtonia flagrans* strain IAH 1297 (identification, stability, manufacturing process, quality control procedures, batch analysis results and analytical methods) and found them to be acceptable.

Based on a review of the data provided by the applicant, the APVMA is satisfied that the chemistry and manufacturing details of *Duddingtonia flagrans* strain IAH 1297 are acceptable.

2.2 Formulated products

The products will be manufactured in Australia in pack sizes ranging from 2 kg to 1000 kg.

The APVMA has evaluated the chemistry aspects of BioWorma and Livamol with BioWorma (stability, formulation, manufacturing process, quality control procedures, specifications, batch analysis results, stability, analytical methods, packaging, and the chemistry aspects of the proposed label) and found them to be acceptable.

BioWorma

DISTINGUISHING NAME:	BioWorma
FORMULATION TYPE:	Free flowing granular meal
ACTIVE CONSTITUENT CONCENTRATION:	*Duddingtonia flagrans* strain IAH 1297 not less than 500,000 chlamydospores per gram

Physical and chemical properties of the formulated product

PHYSICAL FORM:	Granule
COLOUR:	Grey to brown
ODOUR:	Protein meal
PACK SIZES AND MATERIALS:	2 kg LDPE 7.5 kg co-polymer high impact PE pail and lid 10 & 11 kg laminated paper bag 15 kg co-polymer high impact PP pail and lid 20 & 22 kg laminated paper bag 25 kg multi-walled, three ply paper bag 25 kg laminated paper bag 1,000 kg woven PP bulk bag
PRODUCT STABILITY:	Product will remain stable for 24 months when stored at 25–30°C

Livamol with BioWorma

DISTINGUISHING NAME:	Livamol with BioWorma
FORMULATION TYPE:	Free flowing granular meal
ACTIVE CONSTITUENT CONCENTRATION:	*Duddingtonia flagrans* strain IAH 1297 not less than 30,000 chlamydospores per gram

Physical and chemical properties of the formulated product

PHYSICAL FORM:	Granule
COLOUR:	Green
ODOUR:	Protein meal
PACK SIZES AND MATERIALS:	2 kg LDPE 7.5 kg co-polymer high impact PE pail and lid 10 & 11 kg laminated paper bag 15 kg co-polymer high impact PP pail and lid 20 & 22 kg laminated paper bag 25 kg multi-walled, three ply paper bag, 25 kg laminated paper bag 1,000 kg woven PP bulk bag
PRODUCT STABILITY:	Product will remain stable for 24 months when stored at 25–30°C

2.3 Recommendations

Based on a review of the chemistry and manufacturing details provided by the applicant, the registration of BioWorma and Livamol with BioWorma, and approval of the active constituent *Duddingtonia flagrans* strain IAH 1297, are supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The ubiquitous fungus, *Duddingtonia flagrans*, is present in animal faeces, soil and compost where it feeds on parasitic nematodes of grazing animals. *D. flagrans* spores, known as chlamydospores, are robust and can survive passage through the digestive tract of animals to be excreted in faeces, where they then germinate. There are at least 25 characterised isolates of *D. flagrans* in Australia. Genetic characterisation of these isolates show they fall into four major phylogenetic groups.

The Applicant submitted data for both products BioWorma and Livamol with BioWorma. Each product contains the microbial constituent *D. flagrans* strain IAH 1297 chlamydospore preparation but at different concentrations. Livamol with BioWorma is also a nutritional stockfeed supplement. Other than *D. flagrans* strain IAH 1297, the products BioWorma and Livamol with BioWorma, contain constituents that are typically present in a number of stockfeed supplements in Australia.

The products are proposed to be thoroughly mixed with feed or feed supplements, and are recommended to be administered daily. Both products will deliver approximately the same number of viable *D. flagrans* chlamydospores per kg bodyweight.

A package of acute toxicology studies was provided for the *D. flagrans* strain IAH 1297 chlamydospore preparation, and the proposed product Livamol with BioWorma. A pulmonary infectivity and pathogenicity study in rats was also provided for the *D. flagrans* strain IAH 1297 chlamydospore preparation. Notably, no sensitisation studies were provided for the proposed products or *D. flagrans* strain IAH 1297. As *D. flagrans* strain IAH 1297 does not produce secondary metabolites at concentrations in excess of the '*Threshold of Toxicological Concern*' for Cramer class III chemicals (0.015 mg/kg bw/d), no repeat dose studies are required. No genotoxicity studies were provided but since there were no genotoxic structural alerts in the characterised secondary metabolites this was considered acceptable.

D. flagrans strain IAH 1297 has very low toxicity in conventional acute toxicity tests. The organism will not be associated with animal produce and none of its metabolites exceed the Threshold of Toxicological Concern. Consequently the establishment of an Acceptable Daily Intake (ADI), or of an Acute Reference Dose (ARfD), is not required.

The formulated products BioWorma and Livamol with BioWorma were estimated to be of low toxicity as demonstrated by acute oral, dermal and intratracheal administration of various quantities of chlamydospores and the low toxicity of the excipient constituents. They are estimated not to be irritating to the skin of rabbits. However, it cannot be ruled out if they respiratory sensitisers or have the potential to induce a cell mediated immunological response. They are estimated to be slight eye irritants.

3.2 Public health standards

Poisons standard

On 31 October 2017 the Delegate of the Secretary of the Department of Health published a final Scheduling decision to exempt *D. flagrans* strain IAH 1297 from Scheduling in the Poisons Standard. An implementation date of 1 February 2018 was notified for this decision.

Health-based guidance values

The Acceptable Daily Intake (ADI) is that quantity of a compound that can safely be consumed on a daily basis for a lifetime. The Acute Reference Dose (ARfD) is the maximum quantity of a compound that can safely be consumed over a short period of time, usually in one meal or during one day.

D. flagrans is a common environmental organism normally present in grasslands.

The organism *D.flagrans* strain IAH 1297 is not infective or pathogenic, and not toxic in acute toxicity tests. The organism is unlikely to be associated with animal produce and none of its metabolites exceed the threshold of toxicological concern. Consequently the establishment of an Acceptable Daily Intake (ADI), or of an Acute Reference Dose (ARfD), is not required.

4 RESIDUES ASSESSMENT

4.1 Metabolism

Duddingtonia flagrans produces secondary metabolites known as flagranones, which are structurally related to the farnesylated cyclohexanoxides of the oligosporon group produced by the nematode-trapping fungus Arthrobotrys oligospora (Anderson et al. 1999). A study of the secondary metabolites of *D. flagrans* strain IAH 1297 found that it produced a single major metabolite identified was flagranone A. Residues of *D. flagrans* (IAH 1297) or flagranone A are not expected in mammalian food commodities therefore radiolabelled metabolism studies are not considered necessary.

4.2 Residues in foods and animal feeds

Available information indicates that residues of *D. flagrans* IAH 1297 are not of toxicological significance, a Table 5 entry is suitable for the proposed use. The Table 5 entry for *Duddingtonia flagrans* strain IAH 1297 'for control in grazing animals' is considered to be appropriate. The proposed withholding periods of Zero (0) days for milk and meat is considered acceptable and an ESI of ‘Zero (0) Days’ is recommended for the proposed use.

4.3 Dietary risk assessment

A Table 5 entry to the MRL Standard has been recommended to cover the proposed use. The APVMA toxicology assessment concluded that health based guidance values were not necessary. It is therefore not necessary to undertake a dietary risk assessment.

4.4 Recommendations

In considering the application, the following amendments will be made to the APVMA MRL standard:

Table 5

SUBSTANCE	USE
ADD:	
Duddingtonia flagrans strain IAH 1297	For use in grazing animals

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Duddingtonia flagrans is ubiquitous in the environment.

Detectable residues of *D.flagrans* IAH 1297 are not expected to be found in meat, offal or milk as a result of the proposed use. Given that the proposed use involves a naturally occurring organism the risk to trade with respect to residues is low and an Export Slaughter Interval (ESI) of ‘Zero (0) Days’ is considered acceptable.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Use pattern

BioWorma and Livamol with BioWorma are provided as feed supplements and are dosed according to body weight with BioWorma to be fed at 6 g/100 kg bodyweight and Livamol with BioWorma to be fed at 100 g/100 kg bodyweight. Further details are provided on product labels as contained in Section 9.

6.2 Exposure during use

Users of the products will include farmers, farm workers, feedmills, zoo workers, stable workers and other animal owners.

Professional (occupational) use (ie greater number of animals treated) is expected to lead to greater exposure than those using the product for private/small herd use. Exposure to the products may occur when opening the container, scooping contents and mixing with animal feed. The routes of exposure are therefore through dermal, ocular and inhalation contact with the product.

Dermal absorption of active constituents from a granular formulation is expected to be low. In addition, the chlamydospores and associated cell debris of the active constituent is not expected to penetrate the skin. There are no *D. flagrans* strain IAH 1297 secondary metabolites that are predicted to exceed a threshold of toxicological concern.

Both products are granular so the potential for the generation of significant amounts of dust under normal circumstances is likely to be limited. A study conducted according to appropriate guidelines showed BioWorma to be essentially dust free (0.004% w/w liberated as dust). A similar study for Livamol for BioWorma was not available although, Livamol with BioWorma is the same product formulation type. Therefore, Livamol with BioWorma is assumed to have similar dust levels. Overall, given the predicted dustiness levels, the inhalational exposure to both products is likely to be low.

In conclusion, there is little to no potential for systemic exposure to the active constituent for users of the product via dermal, inhalational and ocular exposure. Local exposure is expected to occur through dermal, inhalational and ocular routes but this is predicted to be low and mostly dermal. Similarly, only low exposure is predicted to occur to the excipient constituents in the formulations

BioWorma and Livamol with BioWorma are estimated to have low acute oral, dermal and inhalational toxicity. They are not predicted to be irritating to the skin but are estimated to be slight eye irritants. It cannot be ruled out if the products are respiratory sensitisers or have the potential to induce a cell-mediated immunological response in the respiratory tract. Exposure from dermal, inhalation and ocular routes are estimated to be low, particularly as the products are granular and expected to liberate little dust.

Overall, the risks from acute systemic effects from product use are considered negligible. The risk of eye irritation is considered slight. The potential for respiratory irritation is considered low. However, sensitisation potential cannot be excluded. In particular, respiratory sensitisation could result in a severe adverse effect and therefore this risk is considered moderate to high. Proteinaceous materials are unlikely to cause skin sensitisation so this risk is considered negligible.

6.3 Exposure during re-handling

The products are administered via addition to animal feed. There will be little potential for exposure from handling used feed containers or remaining feed. As the products represent a low hazard (except for possible sensitisation effects) and exposure will be limited, the risk from re-handling is considered negligible.

6.4 Recommendations for safe use

The following first aid instructions and safety directions are recommended for inclusion on the product label:

First aid instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766.

Safety directions

May irritate the eyes, nose and throat. Avoid inhaling dust. When preparing feed wear disposable gloves and disposable dust mask covering the mouth and nose. Wash hands after use.

6.5 Conclusion

The registration of BioWorma and Livamol with BioWorma containing *D. flagrans* strain IAH 1297 as a biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals, is supported from a human health perspective.

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

The following environmental assessment has been conducted for the approval of a new active constituent, *Duddingtonia flagrans* (IAH 1297), and the two products BioWorma and Livamol with Bioworma for use as a biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals.

7.2 Natural occurrence in the environment

D. flagrans is a soil borne organism that occurs world-wide, eg in Australia, New Zealand, Denmark, UK, France, Germany, USA, India, Malaysia, South Africa and China. The species is often found at low population densities in pastures and appears to be associated with the hosts of animal parasitic nematodes (cattle, sheep, goats, horses) and, particularly with their faecal pats, but also occurs in compost, leaf litter, soil, decaying wood, and on pasture.

7.3 Fate in the environment

After application to pasture via sheep faeces in Australia, *D. flagrans* strain IAH 1297 did not spread beyond the point of deposition in the horizontal plane but was observed to penetrate down the soil profile. It is thought that the downwards penetration of *D. flagrans* into the soil was the result of chlamydospore relocation rather than mycelial growth.

D. flagrans strain IAH 1297 will not grow at a distance from faecal pats and will not colonise the soil of pastures. As spore production by *D. flagrans* is very poor, dispersal by spores from faecal pats can be discounted. Accordingly, following administration of *D. flagrans* to grazing animals, it is considered that proliferation in the environment to levels higher than natural background of the species can be excluded.

7.4 Risk assessment

The risk assessment evaluated the potential adverse effects of *Duddingtonia flagrans* strain IAH 1297 to non-target organisms.

Risk to terrestrial vertebrates

Risks to terrestrial vertebrates, such as mammals and birds, are considered to be acceptable as this fungus is not able to germinate under anaerobic conditions and at temperatures above 37ºC. Additionally, it has been used in studies in populations of mammals such as sheep, horses, pigs, cows, dogs and mice with no significant adverse effects.

Risk to aquatic species

Risks to aquatic organisms such as aquatic invertebrates, algae, aquatic plants and fish, are also considered to be acceptable as exposure of these organisms is considered improbable due to the behaviour of the fungi and the proposed use pattern (ie administration with feed from feeding troughs, with the main exposure pathway to the broader environment being through the faeces of treated animals).

Risk to other non-target organisms

It is considered that the risk of *Duddingtonia flagrans* strain IAH 1297 to other non-target organisms that might be exposed (such as terrestrial arthropods, soil organisms, and terrestrial plants) is low due to:

- Widespread natural occurrence of *Duddingtonia flagrans* in the environment.
- Low genetic variation—populations are comparable from one place to another.
- High host specificity—proliferates poorly in natural soils
- Specific nature of 'trap' means lack of effect on non-target organisms
- Preference of *D. flagrans* to colonise faecal pats; the surrounding soil is rarely colonised—the additional *D. flagrans* applied is localised and should not spread beyond the faecal pat.
- No effects were reported in the literature on organisms other than nematodes like insects, earthworms, soil microfauna, and soil fungi.
- Infectivity in warm-blooded animals can also be excluded by the fact that *D. flagrans* spores do not germinate at 37°C or under anaerobic conditions
- Abundance and diversity of soil nematodes were unchanged in soil from paddocks in Sweden, Denmark, Australia, New Zealand, and France where young cattle, sheep or goats treated with *D. flagrans* or untreated animals were grazing—annual variation in population was more influenced by climate than by treatment of grazing animals.
- No effects on non-target arthropods such as dung beetles or on earthworms.
- No effect on dung decomposition which indicates that *D. flagrans* has no significant short-term adverse impact on its immediate micro-environment.
- Infectivity in plants was never observed in spite of its global occurrence and extensive use for more than 30 years.

7.5 Conclusions

The APVMA is satisfied that the proposed use of the products is unlikely to have an unintended effect that is harmful to animals, plants or things or the environment.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed products use patterns

BioWorma and Livamol with BioWorma are palatable feed supplements that contain the spores of *Duddingtonia flagrans* strain IAH 1297, a naturally occurring fungus commonly found in soil and pasture. It is a non-chemical biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals, which acts by substantially reducing the numbers of infective worm larvae (including chemical/anthelmintic multi-resistant larvae) emerging from manure onto pasture.

BioWorma and Livamol with BioWorma are provided as feed supplements and are dosed according to body weight with BioWorma to be fed at 6g/100kg bodyweight and Livamol with BioWorma to be fed at 100 g/100 kg bodyweight. Further details are provided on product labels as contained in Section 9.

8.2 Summary of evaluation of efficacy and target safety

The applicant, International Animal Health Products Pty Ltd, presented results from numerous published references, one dose titration study, 12 dose confirmation studies and three target animal safety studies.

Efficacy

Dose titration studies

One dose titration study conducted in horses was conducted in northern New South Wales.

The study included 20 mares allocated to five treatment groups of four animals based on Day -5 faecal egg count and bodyweight. For each treatment group, fungal spores were blended as required with a commercial horse pellet and fed to the animals daily for four days. Faecal samples were collected from each animal daily for a total of five days. For each day of the experiment triplicate faecal egg counts were performed for each animal using a modified McMaster technique; triplicate faecal cultures (50g) were set-up to estimate the number of larvae emerging from culture and to calculate the percentage of larvae and larval species emerging from culture. Four replicate faecal samples were plated onto agar to establish the presence or absence of *D. flagrans*.

The mean reduction in larval emergence for the five treatment groups over three-four days ranged from 66.2% to 86.6%.

The conclusion of the study was that *D. flagrans* would be appropriate for use as a biological control for nematode parasites in horses.

Dose confirmation studies—Cattle

Two dose confirmation studies were conducted in cattle.

The first study aimed to determine if pasture contamination was reduced by feeding BioWorma to calves with a mixed infection of gastrointestinal nematodes, including known anthelmintic resistant strains. The study was conducted under two different pasture and climatic conditions (New England region and Southern Tablelands regions of NSW) in the spring.

Seven young cattle (2.5–6 months of age) were selected on the basis of known gastrointestinal strongyle burdens, with additional infections applied to ensure a wide range of species were encountered. Animals were offered the control supplement (Livamol) for seven days. Faecal egg counts (FECs) were conducted on each animal and the six animals with the highest FECs selected for the study. Individual faecal samples were collected over a 24-hour period (control samples), faecal egg counts (triplicate) and coprocultures (quadruplicate) were performed and sub-samples of the faeces promptly forwarded for placement onto pasture at each of the two trial sites. The cattle were then offered the test supplement (BioWorma) for a further six days. Individual faecal samples were again collected over a 24 hour period (BioWorma samples) and tested and forwarded for placement onto pasture, as for the control samples above.

At 2–weekly intervals for 8 weeks the remaining faecal material from a randomly selected control and BioWorma faecal pat were collected at each trial site and the number and identity of infective larvae determined by FECs, coproculture and subsequent titration of emerging larvae. In addition, the herbage in a 40 cm circle under and around the pat was removed, washed and the number and identity of bovine-infective nematode larvae determined.

Reductions in cattle strongyle larvae on pasture in BioWorma faeces vs. control faeces were consistent over the 8 weeks of this trial, ranging from 63–84% in New England and 70–100% in the Southern Tablelands site. No adverse events were observed.

The second study aimed to determine if feeding BioWorma to cattle reduces the availability of nematode parasite larvae (including resistant strains) on the pasture surrounding the faecal pats from treated animals during autumn.

Seven calves (7–8 months of age) were selected from a larger group on the basis of known gastrointestinal strongyle burdens and offered the control supplement Livamol for seven days. Each animal's faeces were collected, faecal egg counts (FECs) were performed and the six animals with the highest FECs were selected for the study, including one animal with an ivermectin-resistant parasite. Individual faecal samples were collected over a 3–day period (Control samples), FECs (triplicate) and coprocultures (quadruplicate) were performed and sub-samples were promptly forwarded for placement on pasture at each of the two trial sites (Dayboro, QLD and Armidale, NSW). These cattle were then offered the BioWorma supplement for seven days. Individual faecal samples were again collected over a 3–day period (BioWorma samples). These were tested and forwarded for placement onto pasture at each of the two sites as for the Control samples above.

At each site at 2–weekly intervals for 8 weeks the remaining faecal material from a randomly-selected control and treated faecal pat were removed from the pasture and the number and identity of infective larvae determined by faecal egg count, incubation and culture and titration of emerging larvae. In addition the herbage in a 40 cm radius circle under and around the pat was removed, washed and the number and identity of bovine-infective nematode larvae determined.

Faecal larval cultures yielded a mixture of larvae including *Haemonchus* spp., *Trichostrongylus* spp., *Ostertagia* spp. *Cooperia* spp. and a small percentage of *Oesophagostomum* spp. at both sites.

Trends in cattle strongyle larvae recovered from pasture harvest and wash were similar at both sites, with substantially greater numbers of larvae recovered in the untreated faeces (Livamol) versus the treated faeces (BioWorma). An 82-88% reduction of bovine-infective larvae were found between the two sites in the trial involving BioWorma compared to the controls. Larval numbers at both sites were greatest at weeks 4, 6 and 8. Reductions in cattle strongyle larvae on pasture were consistently high over weeks 4, 6 and 8 at both Dayboro (maximum value 97% at week 8) and Armidale (maximum value 86% at week 8).

Statistical analysis of the two studies combined showed that the treatment of cattle with BioWorma significantly (P=0.006) reduced the detection of cattle parasite larvae on pasture surrounding the faeces of treated animals over an 8–week post-treatment period.

No adverse events were observed.

Dose confirmation studies—Goats

Three dose confirmation studies were conducted in goats.

The first study aimed to determine if feeding BioWorma to goats reduces the availability of nematode parasite larvae (including resistant strains) on the pasture surrounding the faecal pats from treated animals during spring.

Eight young goats (2 years of age) were selected from a larger group and relocated to individual pen facilities. On arrival, goats were weighed and treated with a combination of anthelmintics (levamisole, albendazole and ivermectin) to remove any existing worm burdens. The goats were then artificially-infected with known multi-resistant strongyle strains. The goats were given the control supplement (Livamol) for seven days. Faecal egg counts were conducted on each animal at this time and the six animals with the highest FECs selected for the study. Individual faecal samples were collected over a 24–hour period (control samples), faecal egg counts (triplicate) and coprocultures (quadruplicate) were performed and sub-samples of the faeces promptly forwarded for placement onto pasture at each of the two trial sites (Armidale and Nimmitabel). The goats were then offered the test supplement (BioWorma) for a further seven days. Individual faecal samples were again collected over a 24 hour period (BioWorma samples) and tested and forwarded for placement onto pasture, as for the control samples above.

At each site at 2-weekly intervals for 8 weeks the remaining faecal material from a randomly-selected control and treated faecal pat were removed from the pasture and the number and identity of infective larvae determined by faecal egg count, incubation and culture and titration of emerging larvae. In addition the herbage in a 40 cm radius circle under and around the pat was removed, washed and the number and identity of caprine-infective nematode larvae determined.

The mean pasture larval recovery from BioWorma treated faeces was lower than from faeces not supplemented with BioWorma at the Armidale site, with the average reduction being 85% (range 56% to 100%). In comparison larval pasture recovery from the Nimmitabel site was very low for both BioWorma and Control groups (less than 4% of the Armidale value for the Control group), due to the colder climate, with unseasonably cold weather occurring just after placement of the faecal pats onto pasture. As a result, the study investigator concluded that no conclusion on the efficacy of BioWorma could be drawn from the Nimmitabel site.

No adverse events were observed.

The second study was conducted to a similar protocol as the first study. The aim was to determine if feeding BioWorma to goats reduces the availability of nematode parasite larvae (including resistant strains) on the pasture surrounding the faecal pats from treated animals at two trial sites (Armidale and Dayboro) during autumn.

Treated goats (12) were infected with gastrointestinal strongyle burdens of predominantly multi-resistant *Haemonchus* spp. plus some susceptible *Trichostrongylus* spp. and *Oesophagostomum* spp. Half of these animals were further artificially infected with known resistant strains including multi-resistant *Teladorsagia* spp. and *Trichostrongylus* spp.

Trends in goat strongyle larval recovery from pasture harvest and wash were similar at both sites, with much greater numbers recovered in the untreated groups (Livamol) and minimal numbers recovered in the treated groups (BioWorma). Reductions in goat strongyle larvae on pasture due to BioWorma treatment were consistently high over the 8 weeks of the trial especially at Dayboro (average reduction of 99%, range 97–99%), while at Armidale the corresponding values were slightly lower (average reduction of 81%, range 33–100%).

No adverse events were observed.

The third goat study was also conducted to a similar protocol as the first study. The aim of this study was to determine if feeding BioWorma to goats reduces the availability of nematode parasite larvae (including resistant strains) on the pasture surrounding the faecal pats from treated animals at two trial sites (Nimmitabel and Dayboro) from treated animals during spring.

Eight goats were artificially infected with multi-resistant strongyles (*Teladorsagia* spp. or *Trichostrongylus* spp.) and the remaining four animals were naturally infected with multi-resistant *Haemonchus* spp. and susceptible strains of *Trichostrongylus* spp. and *Oesophagostomum* spp.

Recovery trends were similar at both sites, with greater numbers of larvae recovered in the untreated groups (Livamol) and minimal numbers recovered in the treated groups (BioWorma). Reductions in goat strongyle larvae on pasture due to BioWorma treatment averaged 80% at Dayboro (maximum 94% at week 8) and 98% at Nimmitabel (maximum 100% at week 8).

Statistical analysis of the three studies combined showed that the treatment of goats with BioWorma significantly (P=0.01) reduced the detection of goat parasite larvae on pasture surrounding the faeces of treated animals over an 8–week post-treatment period.

No adverse reactions were observed.

Dose confirmation studies - Horses

Three dose confirmation studies were conducted with horses. The first study assessed the efficacy of BioWorma at reducing the availability of nematode parasite larvae on the pasture surrounding the faecal pats at one trial site (Armidale) in autumn, the second assessed efficacy at two trial sites (Nimmitabel and Armidale) in spring and the third assessed efficacy at two trial sites (Armidale and Dayboro) in autumn.

In each study horses were selected on the basis of known gastrointestinal strongyle burdens. The horses were offered the placebo supplement (Livamol) for seven days. Individual faecal samples were then collected over a 24-hour period (Control samples). The faecal samples were promptly forwarded for placement onto randomly allocated plots on an area of homogenous pasture at the trial sites.

The horses were then offered the test supplement (BioWorma) for a further five days. Individual faecal samples were again collected over a 24 hour period (BioWorma samples) and tested and placed on pasture as for Control samples above.

At each site at 2-weekly intervals for 8 weeks the remaining faecal material from a randomly-selected control and treated faecal pat were removed from the pasture and the number and identity of infective larvae determined by faecal egg count, incubation and culture and titration of emerging larvae. In addition the herbage in a 40 cm radius circle under and around the pat was removed, washed and the number and identity of equine-infective nematode larvae determined.

Nematode species in the studies were cyathostomes, *Strongylus* spp. and *Trichostrongylus axei*.

Statistical analysis of the three studies combined showed that the treatment of horses with BioWorma significantly (P=0.004) reduced the detection of horse parasite larvae on pasture surrounding the faeces of treated animals over an 8-week post-treatment period.

No adverse reactions were observed in any of the treated horses.

Dose confirmation studies - Sheep

Four dose confirmation studies were conducted with sheep. The first study assessed the efficacy of BioWorma at reducing the availability of nematode parasite larvae on pasture at Armidale, NSW in summer, the second assessed efficacy in the Monaro region of NSW in spring/summer, the third assessed efficacy at Armidale, NSW in spring/summer and the fourth assessed efficacy in south east Queensland in summer/autumn. Assessment of efficacy was by conducting total worm counts in tracer sheep that grazed for 21 days on paddocks that had previously been grazed by sheep supplemented with BioWorma at the proposed label dose rate for up to 4 months. Tracer sheep were placed on the study paddocks at the end of the study and, in some of the studies, at a midpoint.

Significant reductions ranging from 57-84% (P<0.05) in worm burdens of the tracer sheep placed in the paddock grazed by BioWorma treated sheep were obtained in all four trials.

No adverse reactions were observed in any of the treated sheep.

Animal target safety

Three target animal safety studies were conducted.

Sheep were administered BioWorma at five times the proposed label dose rate for six weeks.

Cattle were administered BioWorma at 10 times the proposed label dose rate for eight weeks.

Horses were administered BioWorma at 10 times the proposed label dose rate for eight weeks.

In the three studies, safety was assessed by a combination of repeated clinical examinations by veterinarians, bodyweight change over the course of the study and serum biochemistry and haematology compared to placebo-treated animals.

No evidence of toxicity attributable to treatment with BioWorma was observed in the studies.

8.3 Conclusions

The application for registration of Bioworma and Livamol with Bioworma is supported on efficacy and animal target safety grounds when used in accordance with label directions.

9 LABELLING REQUIREMENTS

(DRAFT LABEL, FRONT PANEL)

READ SAFETY DIRECTIONS BEFORE OPENING OR USING
FOR ANIMAL TREATMENT ONLY

LIVAMOL®
with BioWorma®

ACTIVE CONSTITUENT
Each gram contains: Minimum of 30,000 chlamydospores of
***Duddingtonia flagrans* IAH 1297**

Nutritional supplement containing the natural biological control, BioWorma®, that captures and consumes infective worm larvae (including chemical/anthelmintic multi-resistant larvae) within the manure of grazing animals.

Livamol® with BioWorma® is a palatable feed supplement containing the spores of ***Duddingtonia flagrans*** as **BioWorma®**, a naturally occurring fungus commonly found in soil and pasture, which has been combined with **Livamol®** (see below). **BioWorma®** is a non-chemical biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals, which acts by substantially reducing the numbers of infective worm larvae (including chemical/anthelmintic multi-resistant larvae) emerging from manure onto pasture. When fed to animals, the thick-walled spores remain inert (having no effect within the host animal) and resist digestion, passing through into the manure. There they germinate and form trapping organs that capture, paralyse and consume emerging infective worm larvae (including chemical/anthelmintic multi-resistant larvae). The crucial re-infestation stage of the parasites' life cycle is interrupted, reducing the amount of re-infection from contaminated pasture. This interruption of the life cycle significantly reduces parasitic nematodes on pasture. The spores are safe, non-toxic and residue-free.

Livamol® is the ideal delivery vehicle for **BioWorma®**, providing a nutritious base of proteins, energy plus added vitamins and minerals which are important for the development and maintenance of immunity of young, growing and grazing animals. Animals receiving adequate feed, maintaining good condition through good nutrition are better able to cope with parasitism and this has a positive impact on their resistance and resilience to worms.

Livamol® with BioWorma® is fed to grazing animals to reduce nematodes:
The following is a list of roundworms/nematodes trapped by ***Duddingtonia flagrans*** globally and the presence or absence of some of these nematodes may vary from region to region. Additionally there will be mixed infections with several worm species infecting the host at the same time:
Sheep & Goats: Barber's Pole Worm or Wire Worm (*Haemonchus* spp.), Black Scour Worm or Hair Worm (*Trichostrongylus* spp.), Brown Stomach Worm (*Teladorsagia* (*Ostertagia*) spp.), Nodule Worm (*Oesophagostomum* spp.), Thin Necked Intestinal Worm (*Nematodirus* spp.), Hookworm (*Bunostomum* spp.), Intestinal Worm (*Cooperia* spp.), Large-mouthed Bowel Worm (*Chabertia* spp.), *Skrjabinema* spp., Threadworm (*Strongyloides* spp.), Whipworm (*Trichuris* spp.), *Gongylonema* spp.* and *Mecistocirrus* spp.*.
Cattle: Barber's Pole Worm or Wire Worm (*Haemonchus* spp.), Brown Stomach Worm (*Ostertagia* spp.), Black Scour Worm or Hair Worm (*Trichostrongylus* spp.), Hookworm (*Bunostomum* spp.), Intestinal Worm (*Cooperia* spp.), Thread-necked Worm (*Nematodirus* spp.), Nodule Worm (*Oesophagostomum* spp.), Threadworm (*Strongyloides* spp.), *Toxocara vitulorum**, Whipworm (*Trichuris* spp.), *Gongylonema* spp.* and *Mecistocirrus* spp.*
Horses: Large strongyles (large red worms), including *Strongylus* spp., *Triodontophorus* spp. and *Oesophagodontus* spp., small strongyles (small red worms or cyathostomes), including *Cyathostomum* spp., *Cylicocyclus* spp. and *Cylicostephanus* spp., Stomach Hair Worm (*Trichostrongylus axei*), Ascarids (*Parascaris equorum*), Threadworms (*Strongyloides westeri*) and Pinworms (*Oxyuris equi*).

Other grazing animals: including Deer, Alpacas and zoo animals.
There are no negative effects on non-target soil nematodes, earthworms, microarthropods, soil bacteria and fungi. Beneficial insects feeding or breeding on manure (eg dung beetles, fly larvae) are not negatively affected by the presence of ***Duddingtonia flagrans***. Manure decomposition is not altered by the presence of ***Duddingtonia flagrans.***
There have not been any recorded negative impacts on non-target soil nematodes.

2 kg ,7.5 kg,10 kg, 11 kg, 15 kg, 20 kg, 22 kg,25 kg, 1000 kg NET

(DRAFT LABEL, BACK PANEL)

LIVAMOL®
with BioWorma®

Livamol® with BioWorma® is a palatable and nutritious blend of proteins, energy and polyunsaturated oils formulated to improve coat condition and general appearance of all grazing animals. Selected omega-3 fatty acids and high oil protein meals improve coat and skin appearance. Coat colour may be affected by dietary levels of minerals such as zinc, copper and iron. **Livamol® with BioWorma®** has been formulated to supplement the daily intake of protein, fatty acids, vitamins and minerals, including calcium and phosphorus.

INGREDIENTS INCLUDE: Protein & Oilseed Meals, Fish Oil, Molasses and added Vitamins and Minerals.

ADDED CONSTITUENTS PER KG:

Vitamin A (Retinol)	60,000 I.U.
Vitamin D3 (Cholecalciferol)	12,000 I.U.
Vitamin B1 (Thiamine)	1 mg
Vitamin B2 (Riboflavin)	2 mg
Vitamin B6 (Pyridoxine)	1 mg
Vitamin B12 (Cyanocobalamin)	32 µg
Copper (Cu) as sulphate	15.7 mg
Cobalt (Co) as sulphate	80 µg
Iodine (I) as sodium iodide	87 µg
Manganese (Mn) as oxide	104 mg
Zinc (Zn) as oxide	25 mg
Duddingtonia flagrans IAH 1297	30 x 10^6 Chlamydospores

NUTRITIONAL INFORMATION / GUARANTEED ANALYSIS		
Minimum Crude Protein	20 %	
Minimum Crude Fat	5 %	
Minimum Crude Fibre	9 %	
Calcium (Ca)	Min. 4 %	Max. 6 %
Phosphorus (P)	Min. 1.5 %	Max. 2.5 %
Salt	Nil	
Maximum Fluorine (F)	0.025 %	
Average Digestible Energy	11 MJ/kg	

DIRECTIONS FOR USE
Dosage and Administration: Dose **Livamol with BioWorma®** according to bodyweight.
1. For best results, treat animals with a suitable chemical wormer/anthelmintic.
2. Ideally, where possible, move the treated animals onto low worm pasture (that is, pasture that has not been grazed by the same animal species for a minimum 6 weeks).
3. The most worm susceptible are young animals (from 3 months up to 18–24 months of age) and periparturient females as they are the most likely to have less resistance to worm infestation due to low immunity. Pasture contamination by adult stock, even with low faecal egg counts (FEC), should not be underestimated considering the volume of faecal material they place on pasture.
4. Commence daily feeding of **Livamol with BioWorma®** to minimise pasture infectivity and maintain the animal's low worm status. Thoroughly mix **Livamol with BioWorma®** with feed or feed supplements.
5. **Livamol with BioWorma®** will begin to work immediately and for best results may be fed continuously when climatic conditions are conducive to **BioWorma®** and parasitic nematode activity.

6. **Livamol with BioWorma®** is recommended for strategic use during periods when weather conditions are conducive to larval development and transmission onto pasture at temperatures above 5° Celsius (40° Fahrenheit).

7. Use in conjunction with a recommended worm management strategy for your area by contacting your Veterinarian, Animal Health Advisor or Government Advisory groups for a strategic Integrated Parasite Management (IPM) plan. It is important to consider the principles of refugia.

Visit: Australia: www.wormboss.com.au OR New Zealand: http://wormwise.co.nz

8. Faecal egg counts (FECs) may be useful to monitor the effectiveness of the worm management strategy. Other options may include faecal egg count reduction test (FECRT) and/or identifying worm species by using faecal larval cultures (FLC).

DAILY FEEDING RATES

LIVAMOL® with BioWorma® may be mixed with feed, offered by free access alongside other feed or may be used in formulated rations preferably under the direction of a nutritionist or veterinarian.
(A standard coffee mug (300 mL) holds 200 g **LIVAMOL® with BioWorma®**)

Bodyweight * (kg)	**25 kg**	**50 kg**	**100 kg**	**200 kg**	**300 kg**	**400 kg**	**500 kg**
Dosage (g/head/day)	25 g	50 g	100 g	200 g	300 g	400 g	500 g

*Dose according to heaviest animal in the group.
Use additional **100 g for each 100 kg** for animals heavier than **500 kg**.

WITHHOLDING PERIODS: MEAT: Zero (0) days, MILK: Zero (0) days.

TRADE ADVICE: EXPORT SLAUGHTER INTERVAL (ESI): NIL

SAFETY DIRECTIONS: May irritate the eyes, nose and throat. Avoid inhaling dust. When preparing feed wear disposable gloves and disposable dust mask covering the mouth and nose. Wash hands after use.

FIRST AID: If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766**.**

ADDITIONAL USER SAFETY INFORMATION: Additional information is listed in the safety data sheet available from International Animal Health Products Pty Ltd.

DISPOSAL [*for paper or cardboard containers and paper material bags***]:** Shake container into medicated feed. Do not dispose of undiluted chemicals on-site. Break, crush, or puncture container and deliver to an approved waste management facility. If an approved waste management facility is not available, bury the punctured containers 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.

DISPOSAL [*for plastic containers*]**:** Triple-rinse container into the medicated feed. Do not dispose of undiluted chemicals on-site. If recycling, replace cap and return clean container to recycler or designated collection point. If not recycling, break, crush, or puncture container and deliver to an approved waste management facility. If an approved waste management facility is not available, bury the broken, crushed or punctured containers 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.

DISPOSAL [*for plastic bags*]: Single-rinse or shake container into the medicated feed. Do not dispose of undiluted chemicals on-site. Puncture bag and deliver to an approved waste management facility. If an approved waste management facility is not available, bury the container 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.

STORAGE: Store below 30ºC (Room Temperature). KEEP OUT OF REACH OF CHILDREN.
Keep container tightly closed in a moisture free environment.

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18 Healey Circuit, Huntingwood, NSW 2148 Australia
Telephone: (61) (2) 96727944 **Fax:** (61) (2) 96727988
Emergency Contact: Poisons Information Centre. *Phone Australia 131 126; New Zealand (0800 POISON) 0800 764 766*.
Website: www.iahp.com.au **Email:** info@iahp.com.au

APVMA Approval No.: XXXXX/XXXXX

Batch No:
Expiry Date:

READ SAFETY DIRECTIONS BEFORE OPENING OR USING
FOR ANIMAL TREATMENT ONLY

BioWorma®

ACTIVE CONSTITUENT:
Each gram contains: Minimum of 500,000 chlamydospores of *Duddingtonia flagrans* IAH 1297

(i) **Natural biological control that captures and consumes infective worm larvae (including chemical/anthelmintic multi-resistant larvae) within the manure of grazing animals**

BioWorma® is a palatable feed supplement that contains the spores of ***Duddingtonia flagrans,*** a naturally occurring fungus commonly found in soil and pasture. It is a non-chemical biological control for the free-living stages of parasitic gastrointestinal nematodes of grazing animals, which acts by substantially reducing the numbers of infective worm larvae (including chemical/anthelmintic multi-resistant larvae) emerging from manure onto pasture. When fed to animals, the thick-walled spores remain inert (having no effect within the host animal) and resist digestion, passing through into the manure. There they germinate and form trapping organs that capture, paralyse and consume emerging infective worm larvae (including chemical/anthelmintic multi-resistant larvae). The crucial re-infestation stage of the parasites' life cycle is interrupted, reducing the amount of re-infection from contaminated pasture. This interruption of the life cycle significantly reduces parasitic nematodes on pasture.
The spores are safe, non-toxic and residue-free.

BioWorma® is fed to grazing animals to reduce nematodes.
The following is a list of roundworms/nematodes trapped by ***Duddingtonia flagrans*** globally and the presence or absence of some of these nematodes may vary from region to region. Additionally there will be mixed infections with several worm species infecting the host at the same time:
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Horses: Large strongyles (large red worms), including *Strongylus* spp., *Triodontophorus* spp. and *Oesophagodontus* spp., small strongyles (small red worms or cyathostomes), including *Cyathostomum* spp., *Cylicocyclus* spp. and *Cylicostephanus* spp., Stomach Hair Worm (*Trichostrongylus axei*), Ascarids (*Parascaris equorum*), Threadworms (*Strongyloides westeri*) and Pinworms (*Oxyuris equi*).
Other grazing animals: including Deer, Alpacas and zoo animals.
There are no negative effects on non-target soil nematodes, earthworms, microarthropods, soil bacteria and fungi. Beneficial insects feeding or breeding on manure (eg dung beetles, fly larvae) are not negatively affected by the presence of ***Duddingtonia flagrans***. Manure decomposition is not altered by the presence of ***Duddingtonia flagrans.***

There have not been any recorded negative impacts on non-target soil nematodes.

2 kg ,7.5 kg,10 kg, 11 kg, 15 kg, 20 kg, 22 kg,25 kg, 1000 kg NET

(DRAFT LABEL, BACK PANEL)

DIRECTIONS FOR USE

Dosage and Administration: Dose **BioWorma**® according to bodyweight.

9. For best results, treat animals with a suitable chemical wormer/anthelmintic.
10. Ideally, where possible, move the treated animals onto low worm pasture (that is, pasture that has not been grazed by the same animal species for a minimum 6 weeks).
11. The most worm susceptible are young animals (from 3 months up to 18–24 months of age) and periparturient females as they are the most likely to have less resistance to worm infestation due to low immunity. Pasture contamination by adult stock, even with low faecal egg counts (FEC), should not be underestimated considering the volume of faecal material they place on pasture.
12. Commence daily feeding of **BioWorma**® to minimise pasture infectivity and maintain the animal's low worm status. Thoroughly mix **BioWorma**® with feed or feed supplements.
13. **BioWorma**® will begin to work immediately and for best results may be fed continuously when climatic conditions are conducive to **BioWorma**® and parasitic nematode activity.
14. **BioWorma**® is recommended for strategic use during periods when weather conditions are conducive to larval development and transmission onto pasture at temperatures above 5° Celsius (40° Fahrenheit).
15. Use in conjunction with a recommended worm management strategy for your area by contacting your Veterinarian, Animal Health Advisor or Government Advisory groups for a strategic Integrated Parasite Management (IPM) plan. It is important to consider the principles of refugia.
    Visit: Australia: www.wormboss.com.au OR New Zealand: http://wormwise.co.nz
16. Faecal egg counts (FECs) may be useful to monitor the effectiveness of the worm management strategy. Other options may include faecal egg count reduction test (FECRT) and/or identifying worm species by using faecal larval cultures (FLC).

DAILY FEEDING RATES							
Bodyweight* (kg)	**25 kg**	**50 kg**	**100 kg**	**200 kg**	**300 kg**	**400 kg**	**500 kg**
Dosage (grams per head per day)	1.5 g	3 g	6 g	12 g	18 g	24 g	30 g

*Dose according to heaviest animal in the group.

Use additional **6 g for each 100 kg** for animals heavier than **500 kg**.

WITHHOLDING PERIODS: MEAT: Zero (0) days, MILK: Zero (0) days.

TRADE ADVICE: EXPORT SLAUGHTER INTERVAL (ESI): NIL

SAFETY DIRECTIONS: May irritate the eyes, nose and throat. Avoid inhaling dust. When preparing feed wear disposable gloves and disposable dust mask covering the mouth and nose. Wash hands after use.

FIRST AID: If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766**.**

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STORAGE: Store below 30 ˚C (Room Temperature). KEEP OUT OF REACH OF CHILDREN.
Keep container tightly closed in a moisture free environment.

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Website: www.iahp.com.au **Email:** info@iahp.com.au

APVMA Approval No.: XXXXX/XXXXX

Batch No.:
Expiry Date:

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
ai	active ingredient
ARfD	Acute Reference Dose
bw	bodyweight
°C	Degrees Celsius
CFU	Colony Forming Units
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EI	Export Interval
ESI	Export Slaughter Interval
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare

HDPE	High Density Polyethylene
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
HQ	Hazard Quotient
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
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
LOD	Limit of Detection—level at which residues can be detected
LOQ	Limit of Quantitation—level at which residues can be quantified
LR_{50}	Lethal rate that kills 50% of the test population of organisms
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NOEC/NOEL	No Observable Effect Concentration/Level
NOAEL	No Observed Adverse Effect Level

OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SDS	Safety Data Sheet
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
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
Ubiquitous	Present, appearing or found everywhere

REFERENCES

EFSA 2006, Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on the safety of the micro-organism preparation of *Duddingtonia flagrans*, for use as a feed additive for calves in accordance with Council Directive 70/524/EEC. The EFSA Journal 334, 1–8.