Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

# Re-evaluation Note REV2006-10

## Re-evaluation of *Colletotrichum gloeosporioides* f.sp. *malvae [CGM]*

The purpose of this Re-evaluation Note is to inform the registrant, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has re-evaluated the active ingredient *Colletotrichum gleosporioides* f.sp. *malvae* and its associated use as a mycoherbicide providing postemergent control of round-leaved mallow *(Malva pusilla*) in field crops.

*Colletotrichum gloeosporiodes* f.sp. *malvae* (CGM) was first registered in 1992 in Canada; therefore, this product is subject to re-evaluation according to Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program* (30 March 2001). The data the PMRA examined for the initial registration of CGM were found to have been reviewed using current scientific approaches. Based on this, the PMRA has determined CGM is expected to pose minimal risk to human health and the environment and is acceptable for continued registration.

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## 1.0 Background

In Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, the Pest Management Regulatory Agency (PMRA) announced that all pesticides, both active ingredients and formulated end-use products, that were registered prior to 31 December 1994 would be re-evaluated to ensure that their continued acceptability is examined using current scientific approaches. *Colletotrichum gloeosporiodes* f.sp. *malvae* (CGM) was first registered in 1992 in Canada; therefore, this product requires re-evaluation.

The data submitted when CGM was registered were re-examined using current scientific approaches presented in the most recent guidelines for microbial pest control agents, Regulatory Directive DIR2001-02, *Guidelines for the Registration of Microbial Pest Control Agents and Products.* Literature searches were also conducted for any published data on the fungal pathogen since initial registration.

According to Regulatory Directive DIR2001-02, the major human health concerns for microbial pest control agents (MPCA) active ingredients are pathogenicity, infectivity/unusual persistence and toxicity of the MPCA and associated by-products, including contaminant microorganisms. Also, the manufacturing methods and quality assurance program should be described in sufficient detail to validate claims regarding the integrity of the MPCA as well as product specifications, including potency, ingredient limits and acceptable contaminant levels, both prior to registration and during the manufacture of products intended for commercial use.

Data submitted to satisfy Part 8, Environmental Fate, of DIR2001-02 are intended to demonstrate whether an MPCA is capable of surviving or replicating in the environment to which it is applied. Environmental fate tests further provide an indication of which non-target organism(s) may be exposed to the MPCA as well as provide an indication of the extent of exposure.

Part 9, Environmental Toxicology, of Regulatory Directive DIR2001-02 prescribes the data requirements for assessing the potential environmental hazards of the MPCA on non-target organisms. The PMRA requires hazard data to predict possible adverse effects of MPCAs and added ingredients in end-use products, i.e., formulants, on broad groups of non-target organisms such as birds, mammals, fish, arthropods, non-arthropod invertebrates, microorganisms and plants.

## 2.0 Re-evaluation of CGM

### 2.1 Identity of the Active Substance

CGM is a naturally occurring fungal pathogen that was originally isolated in Regina, Saskatchewan, from round-leaved mallow displaying anthracnose symptoms in greenhouse tests. A culture of this strain has been deposited in the American Type Culture Collection (ATCC) on 7 August 1985 and assigned the Accession Number 20767.

| | |
|---|---|
| Common name: | *Colletotrichum gloeosporiodes* f.sp. *malvae* |
| Biological name: | *Colletotrichum gloeosporiodes* f.sp. *malvae* American Type Culture Collection # 20767 |
| Biological family: | Melanconiaceae |
| Function: | Mycoherbicide |
| Basic manufacturer: | Philom Bios |

The currently registered commercial end-use product, BioMal®, is a wettable powder formulated with CGM spores only that provides postemergent control of round-leaved mallow (*Malva pusilla*) in field crops. These crops include wheat, rye, flax, lentil, barley, canola, sunflower, soybean, oats, mustard, sugar beet and buckwheat. Application is proposed to be by conventional field spraying equipment (including backpack equipment) at a rate of 100–150 L/ha, after the second-leaf stage, but before the mallow is 15 cm tall. A rate of $1 \times 10^{11}$ viable spores is required to treat 1 ha. Aerial application is prohibited.

### 2.2 Re-evaluation

The manufacturing process and quality assurance program was described in sufficient detail for BioMal® at the time of initial registration; they fulfil the requirements under Part 2, Product Characterization and Analysis, of DIR2001-02. However, submission of quality assurance data including potency (biological activity) of the active ingredient and screening for microbiological contaminants from five production runs remains outstanding.

Data submitted for the initial registration were considered to meet the current data requirements for mycoherbicides and adequately address major concerns for human health from use of BioMal®. Based on data for infectivity, pathogenicity and acute toxicity studies, BioMal® is not infectious in the rat, is a skin sensitizer and is capable of inducing the formation of CGM antigen related pulmonary granulomas. The current

BioMal® label must be amended to be consistent with current MPCA labels (see Section 4.0), including personal protective equipment.

Based on test data that were reviewed for the initial registration decision on BioMal®, the requirements for environmental fate and environmental toxicology of DIR2001-02 have been satisfied. BioMal® is not expected to pose a risk to birds and mammals. A 15-m buffer zone is required to protect aquatic habitats because the data were insufficient to determine the risk to aquatic plants. Based on data from an aquatic microcosm study involving fish, amphipods and bivalves, BioMal® does not appear to be toxic or pathogenic to freshwater fish or freshwater invertebrates.

A current review of the scientific literature indicated that *Nicotiana* species (tobacco) may be susceptible to infection by a strain considered to be very similar to CGM (Shen, Goodwin and Hsiang 2001). Although plant testing data submitted when CGM was first registered included members of the Solanaceae family (i.e., tomato), testing did not include tobacco. Based on this, the PMRA requires the BioMal® label to indicate potential risk/crop injury to tobacco crops from spray drift.

It appears from the published scientific literature that the reported incidences of *Colletotrichum* species causing infection in non-target organisms other than plants have increased in recent years (Mendiratta et al. 2005, O'Quinn et al. 2001, Manire et al. 2002). Upon closer examination of the literature, the causative agent was found not to be CGM. However, there was one reported case where the fungal pathogen was identified as *Colletotrichum gleosporiodes* (*forma specialis* not given) and involved an immunocompromised individual that suffered a localized infection around a puncture wound from a cactus thorn (O'Quinn et al. 2001). Thus, indications are that while immunosuppressed individuals may be susceptible to localized infections by this species, the general population is not likely to be at risk to this common soil microorganism.

## 3.0 Re-evaluation Decision

The data that were submitted to PMRA for the initial registration of the end-use product of CGM, BioMal®, satisfy the current data requirements for mycoherbicides. The scientific approaches used to assess these data and to draw conclusions on the safety, merit and value of BioMal® are also considered to meet current standards.

Based on this, PMRA has determined that BioMal® is expected to pose minimal risk to human health and the environment. BioMal® is acceptable for continued registration with the implementation of the mitigation measures specified in Section 4.0. The registrant is required to submit the data identified in Section 5.0.

## 4.0 Regulatory Actions

The Canadian label for BioMal® must be updated to current wording and include the following statements.

The registrant is required to add the following to the **principal display panel** of the BioMal® label.

> POTENTIAL SENSITIZER
>
> **FIRST AID:**
> If swallowed: Rinse mouth and throat with copious amounts of water. Do not induce vomiting.
> If on skin/clothing: Take off contaminated clothing. Wash with plenty of soap and water.
> If inhaled: Move to fresh air.
> If in eyes: Hold eye open and rinse slowly and gently with water. Remove contact lenses, if present, then continue rinsing eye.
> General: Seek medical attention immediately if irritation or signs of toxicity occur and persist or are severe. Take container, label or product name and Pest Control Product Registration Number with you when seeking medical attention.
>
> **TOXICOLOGICAL INFORMATION:**
> Treat symptomatically.

The registrant is required to update the current guarantee statement on the **principal display panel** of the BioMal® label from:

> This product is guaranteed to contain $10^{11}$ viable spores of *Colletotrichum gleosporiodes* f.sp. *malvae* in the quantity of product required to treat 1 ha (~2.5 acres).

to:

> This product is guaranteed to contain $10^{11}$ viable spores of *Colletotrichum gleosporiodes* f.sp. *malvae ATCC* strain 20767 in the quantity of product required to treat 1 ha.

In the **DIRECTIONS FOR USE** section of the label for BioMal®:

> DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty.
>
> Field sprayer application: DO NOT apply with spray droplets smaller than the ASAE medium classification.

In the **PRECAUTIONS** section of the secondary display panel for BioMal®:

> May cause sensitization. Avoid contact with skin, eyes or clothing. Avoid inhalation of spray mist. All handlers must wear a long-sleeved shirt, long pants, waterproof gloves, shoes plus socks and eye goggles, and a dust/mist filtering respirator (MSH/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products, when handling, mixing/loading or applying the product and during all clean-up/repair activities. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.

In the **ENVIRONMENTAL HAZARD** section of the label for BioMal®:

> To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g., soils that are compacted or fine textured such as clay).
>
> Avoid application of this product when heavy rain is forecast.
>
> Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.
>
> DO NOT apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands), estuaries or marine habitats.
>
> DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

The BioMal® leaflet must advise users of the following:

- that crop injury may occur to tobacco crops planted in the vicinity of the fields being treated with BioMal®.

The label amendments presented above do not include all label requirements for the end-use product, such as first aid statements, disposal statements, precautionary statements, and supplementary protective equipment. Additional information on labels of the currently registered product should not be removed unless it contradicts the above label statements.

## 5.0 Data Requirements

The registrant is required to submit quality assurance data including potency (biological activity) of the active ingredient and screening for microbiological contaminants of five production runs.

## References

Manire, A.C., et al. 2002. Desseminated Mycotic Infection Caused by *Colletotrichum acutatum* in a Kemp's Ridley Sea Turtle (*Lepidochelys kempi*). *Journal of Clinical Microbiology*. November 2002. p. 4273–4280.

Mendiratta, D.K., et al. 2005. Keratitis due to *Colletotrichum dematium*–A case report. *Indian Journal Medical Microbiology*. January–March 2005. 23(1):56–8.

O'Quinn, R.P., et al. 2001. *Colletotrichum* species as emerging opportunistic fungal pathogens: A report of 3 cases of phaeohyphomycosis and review. *Journal of the Amercian Academy of Dermatology*. July 2001. 45(1):56–61.

Shen, S., P.H. Goodwin and T. Hsiang. 2001. Infection of *Nicotiana* species by anthracnose fungus, *Colletotrichum orbiculare*. *European Journal of Plant Pathology*. Kluwer Academic Publishers. 107:767–773.