



## Evaluation Report for Category B, Subcategory 2.3, 3.6 Application

**Application Number:** 2013-4073  
**Application:** Changes End-Use Product Chemistry-Identity of Formulants, and New or Changes to Product Labels  
**Product:** Zivion M  
**Registration Number:** 30521  
**Active ingredients (a.i.):** Natamycin  
**PMRA Document Number :** 2452877

### Purpose of Application

The purpose of this application was to amend the Zivion M label by reducing the pre-harvest interval, shortening the compost and casing steaming time before disposal, and changing the formulation. This product is used for the suppression of Dry Bubble Disease, *Verticillium fungicola* on cultivated mushrooms, *Agaricus bisporus*.

### Chemistry Assessment

Zivion M is formulated as a suspension containing natamycin at nominal concentration of 10.34%. This end-use product has a density of 1.08 g/mL and pH of 4.74-5.03. The chemistry requirements for this product have been fulfilled.

### Health Assessments

Natamycin (98%) was of low toxicity via the oral ( $LD_{50} > 2000$  mg/kg bw), dermal ( $LD_{50} > 5050$  mg/kg bw) and inhalation routes ( $LC_{50} > 2.39$  mg/L) when administered to rats. It was severely irritating to the eyes and slightly irritating to the skin of rabbits. Natamycin technical grade active ingredient (TGAI) is not considered a dermal sensitizer.

A data waiver rationale was submitted requesting that the acute toxicity, irritation and sensitization studies submitted in support of Natamycin TGAI be used to fulfill the toxicology data requirements for the previous formulation of Zivion M, with the exception of primary eye irritation for which data was submitted. The primary eye irritation study submitted for the previous formulation of Zivion M categorized it as non- to minimally irritating to the eyes.

The formulation change for Zivion M and resulting changes in pH (from 6.5 to 4.74–5.03) and viscosity (from 2200 mPa·s to 1094–1477 mPa·s at 20°C) are not expected to pose any additional toxicity or irritation concerns. At the low end, the pH of the new formulation is in the range of natural skin pH (estimated average of 4.7) and is within the pH range of finished water (pH 5.0–10.5).

Occupational exposure to Zivion M may occur during mixing, loading, application and post-

application activities (e.g., clean-up and repair, harvesting, handling of treated compost and casing). Occupational exposure will be limited with the use of appropriate personal protective equipment and hygiene statements on the label.

Bystander exposure is not expected to occur as the use of Zivion M will be in a closed growing house where bystanders are not expected to be present.

Food residue exposure to natamycin from consumption of treated mushrooms is not expected to be of concern as conservative exposure estimates show that it will not appreciably increase the dietary exposure to natamycin beyond what is currently expected from its use as a food additive. The maximum level of natamycin detected in mushroom harvested six hours after a total of four applications (5.43 ppm) is lower than the level permitted for use on cheese (10–20 ppm; Health Canada *Food and Drug Regulations*) and cured meats (6–20 ppm). The level of natamycin residues should be lower with fewer applications (maximum of two). Furthermore, results from a previously submitted residue study demonstrated that washing will further greatly reduce the natamycin residues on treated mushrooms.

Zivion M is applied in a closed growing house and the level of natamycin residues in treated compost and casing is sufficiently reduced by 12 hours of steaming prior to disposal (PMRA# 2330473). Therefore, exposure to natamycin in drinking water is likely to be negligible.

### **Maximum Residue Limit**

As the proposed use of Zivion M at the maximum application rate on white button mushrooms and with a pre-harvest interval (PHI) of six hours is not expected to appreciably increase the dietary exposure to natamycin above levels which are currently expected from its use as a food additive, it is not necessary to establish a maximum residue limit (MRL) for natamycin.

### **Environmental Assessment**

A new residue trial, conducted to support the revised steaming time, was reviewed. Steaming times of 8, 12, and 16 hours were compared for the casing and the compost. Casing samples had the highest average residue of 4.33 ppm at pre-steam, but these residues rapidly declined to an average of 0.36 after 12 hours and 0.11 ppm after 16 hours of steaming. While very limited amounts of natamycin were found in the compost at pre-stream (0.06 ppm), these residues rapidly declined to an average of 0.01 ppm after 12 hours, and had declined after 16 hours of steaming to below the limit of quantitation, 0.01 ppm. Based on the results of this study, the reduction of the steaming time from 24 to 12 hours is not expected to increase the environmental exposure of natamycin via spent compost.

### **Value Assessment**

Based on the similarity of the proposed formulation to the previous formulation, no value information was required in support of the formulation change.

### **Conclusion**

The Pest Management Regulatory Agency has completed an assessment of the information provided in support of the product, Zivion M, and has found the information sufficient to support the change in formulation and modify the label for its use on cultivated mushrooms.

## References

PMRA Document Number	Reference
1907399	2010, Natamycin L Enforcement Analytical Method, DACO: 3.4.1
1907401	[Privacy Information Removed], 2010, Natamycin L Chemical and Physical Properties, DACO: 3.5,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14, 3.5.15,3.5.2,3.5.3,3.5.4, 3.5.5,3.5.6,3.5.7,3.5.8,3.5.9
1907402	2010, Natamycin L Storage Stability and Corrosion Characteristics, DACO: 3.5.10, 3.5.14
2003917	2011, Natamycin L (Submission No. 2010-2330): Request for Clarification, DACO: 3.2.2,3.5.10,3.5.14 CBI
2003919	2011, Spec Sheet Foam Control 30, DACO: 3.2.2 CBI
2020626	2011, 12-Month Stability Study Report on Natamycin L, DACO: 3.5.10,3.5.14
2077272	2011, 18- Month Storage Stability and Corrosion Characteristics, DACO: 3.5.10, 3.5.14
2129343	2011, 2010-2330 Notification, DACO: 3.5.10
2136240	2011, External Standard Retention Time behavior - email, DACO: 3.5.10
2360976	2013, Product Identification, Formulants, Formulation Process and Certified Limits, DACO: 3.1,3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1
2360977	2013, Product Identification, Formulants, Formulation Process and Certified Limits, DACO: 3.1,3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1 CBI
2360983	2013, Measurements Viscosity, Density and pH, DACO: 3.5.6,3.5.7,3.5.9
2330473	2013, Natamycin Residue Analysis in Mushrooms, Compost and Casing, DACO: 7.4.1.
1907410	2010, Petition Proposing an Exemption from Tolerance for Pesticide Residues of Natamycinin in or on Mushrooms, DACO: 7.8
1907411	2010, Request for Waiver of 5 Acute Toxicity Tests Non CBI, DACO: 4.2.1,4.2.2,4.2.3,4.2.4,4.2.5,4.2.6,4.6
1907412	2010, Request for Waiver of 5 Acute Toxicity Tests CBI, DACO: 4.6.1,4.6.2,4.6.3,4.6.4,4.6.5,4.6.6 CBI
1907413	2009, Acute Eye Irritation Study in Rabbits, DACO: 4.6.4
1922392	2010, DACO 4.2.9 Other Acute Studies, DACO: 4.2.9
2330470	2013, Letter to R. Aucoin, DACO: 0.8
2360979	2013, Letter to Marion Law, DACO: 0.8
2360981	2013, Zivion M Use Description Scenario, DACO: 5.2
2487172	2014, Request for Waiver of 6 Acute Toxicity Tests, DACO: 4.6 CBI

## Additional Information Considered

## Published Information

## **Human and Animal Health**

PMRA

Document

Number

2388635

Reference

CODEX GENERAL STANDARD FOR FOOD ADDITIVES. CODEX  
STAN 192-1995 PREAMBLE, DACO: 12.5

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