



This document is scheduled to be published in the Federal Register on 05/18/2012 and available online at <http://federalregister.gov/a/2012-12105>, and on [FDsys.gov](http://FDsys.gov)

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## **ENVIRONMENTAL PROTECTION AGENCY**

### **40 CFR Part 180**

**[EPA-HQ-OPP-2010-0727; FRL-9349-2]**

### **Natamycin; Exemption from the Requirement of a Tolerance**

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Final rule.

**SUMMARY:** This regulation establishes an exemption from the requirement of a tolerance for residues of the biochemical, natamycin, in or on mushrooms when applied as a fungistat to prevent the germination of fungal spores on mushrooms produced in mushroom production facilities. DSM Food Specialties B.V. (DSM) submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for such residues of natamycin.

**DATES:** This regulation is effective [*insert date of publication in the Federal Register*]. Objections and requests for hearings must be received on or before [*insert date 60 days after date of publication in the Federal Register*], and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the

**SUPPLEMENTARY INFORMATION).**

**ADDRESSES:** The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2010-0727; FRL-9349-2, is available either electronically through <http://www.regulations.gov> or in hard copy at the OPP Docket in the Environmental Protection Agency Docket Center (EPA/DC), located in EPA West, Rm. 3334, 1301 Constitution Ave. NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805. Please review the visitor instructions and additional information about the docket available at <http://www.epa.gov/dockets>.

**FOR FURTHER INFORMATION CONTACT:** Cheryl Greene, Biopesticides and Pollution Prevention Division (7511P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 308-0352, email address: [green.cheryl@epa.gov](mailto:green.cheryl@epa.gov).

**SUPPLEMENTARY INFORMATION:**

**I. General Information**

*A. Does this Action Apply to Me?*

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

*B. How Can I Get Electronic Access to Other Related Information?*

You may access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's e-CFR site at

*<http://ecfr.gpoaccess.gov/cgi/t/text/text->*

*[idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab\\_02.tpl](http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl)*. To access the harmonized test guidelines referenced in this document electronically, please go to

*<http://www.epa.gov/ocspp>* and select “Test Methods and Guidelines.”

*C. How Can I File an Objection or Hearing Request?*

Under FFDCFA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2010-0727 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before *[insert date 60 days after date of*

*publication in the Federal Register*]. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing that does not contain any CBI for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit a copy of your non-CBI objection or hearing request, identified by docket ID number EPA-HQ-OPP-2010-0727, by one of the following methods:

- *Federal eRulemaking Portal*: <http://www.regulations.gov>. Follow the online instructions for submitting comments.

- *Mail*: Office of Pesticide Programs (OPP) Regulatory Public Docket (7502P), Environmental Protection Agency, 1200 Pennsylvania Ave., NW. Washington, DC 20460-0001.

- *Delivery*: OPP Regulatory Public Docket (7502P), Environmental Protection Agency, Rm. S-4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. Deliveries are only accepted during the Docket Facility's normal hours of operation (8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays). Special arrangements should be made for deliveries of boxed information. The Docket Facility telephone number is (703) 305-5805.

## **II. Background and Statutory Findings**

In the **Federal Register** of April 20, 2011, (76 FR 22067)(FRL-8869-7), EPA issued a notice pursuant to section 408(d)(3) of FFDCA, 21 U.S.C. 346a(d)(3), announcing the notice of filing of a pesticide tolerance petition (PP 0F7729), by DSM

Food Specialties B.V. (DSM), Alexander Fleminglaan 1, 2613 AX Delft, The Netherlands, c/o Keller and Heckman, LLP, 1001 G. Street, NW., Washington, D.C. 20001. The petition requested that 40 CFR part 180 be amended by establishing an exemption from the requirement of a tolerance for residues of natamycin in or on mushrooms when applied as a fungistat to mushrooms produced in an enclosed mushroom production facility. This notice referenced a summary of the petition prepared by the petitioner which is available in the docket (EPA-HQ-OPP-2010-0727) at <http://www.regulations.gov>. There were no comments received in response to the notice of filing.

Section 408(c)(2)(A)(i) of FFDCFA allows EPA to establish an exemption from the requirement for a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the exemption is “safe.” Section 408(c)(2)(A)(ii) of FFDCFA defines “safe” to mean that “there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.” This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Pursuant to section 408(c)(2)(B) of FFDCFA, in establishing or maintaining in effect an exemption from the requirement of a tolerance, EPA must take into account the factors set forth in section 408(b)(2)(C) of FFDCFA, which require EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to “ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....” Additionally, section 408(b)(2)(D) of FFDCFA requires that the

Agency consider “available information concerning the cumulative effects of a particular pesticide's residues” and “other substances that have a common mechanism of toxicity.”

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. First, EPA determines the toxicity of pesticides. Second, EPA examines exposure to the pesticide through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings.

### **III. Toxicological Profile**

Consistent with section 408(b)(2)(D) of FFDCA, EPA has reviewed the available scientific data and other relevant information in support of this action and considered its validity, completeness, and reliability and the relationship of this information to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

Natamycin is a naturally occurring antimicrobial compound derived from the common soil microorganisms, *Streptomyces natalensis*, *Streptomyces lydicus*, and *Streptomyces chattanoogensis*. Natamycin was originally discovered in *Streptomyces natalensis* in South Africa in the early 1950s, and was subsequently discovered to also occur naturally in North America in *Streptomyces lydicus* and *Streptomyces chattanoogensis*. It is commercially produced by a submerged oxygen-based fermentation of *Streptomyces natalensis*, *Streptomyces lydicus*, or *Streptomyces chattanoogensis*. As a biochemical pesticide active ingredient, natamycin is intended for use as a fungistat to prevent and control the germination of mold and yeast spores in the growth media of mushrooms produced in enclosed mushroom production facilities. Natamycin has a non-toxic mode of action, has no effects on fungal mycelia, and

development of antibiotic resistance to natamycin has not been reported during its entire history of use.

Natamycin has been used as a food preservative worldwide for over 40 years (Ref.1) and is approved as a food additive/preservative by the European Union, the World Health Organization, and individual countries including New Zealand and Australia for use as a fungistat to suppress mold on cheese, meats and sausage. In the United States, natamycin is approved by the Food and Drug Administration (FDA) as a direct food additive/preservative for the inhibition of mold and yeast on the surface of cheeses (21CFR 172.155) and as an additive to the feed and drinking water of broiler chickens to retard the growth of specific molds (21CFR 573.685). Natamycin is also FDA approved for use as a treatment to suppress fungal eye infections such as blepharitis, conjunctivitis, and keratitis.

EPA has evaluated the available toxicity data on natamycin and considered their validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children, to natamycin. Specific information on the studies and information received and reviewed, the nature of adverse effects caused by natamycin as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies and information are discussed in this unit.

1. *Acute toxicity (MRIDs 48105505 through 48105510).* The natamycin Technical Grade Active Ingredient (TGAI) is classified in Toxicity Category III for acute oral toxicity, and Toxicity Category IV for acute dermal toxicity, acute inhalation

toxicity, primary eye irritation, and primary dermal irritation. Natamycin is not a sensitizer.

2. *Subchronic toxicity (MRID 48105511)*. Subchronic (rat) feeding studies demonstrate that the LOAEL was 2,000 parts per million (ppm) in the diet (204 milligrams/kilogram of body weight per day (mg/kg bw/day) for males and 238 mg/kg bw/day for females) based on significantly lower body weight. The NOAEL was 500 ppm in the diet (42 mg/kg bw/day for males and 48 mg/kg bw/day for females).

Natamycin is not a mutagen and is not cytotoxic. Subchronic (90-day) dermal toxicity and subchronic inhalation studies were not submitted, but are not required based on a lack of repeated exposure to workers and applicators via these two routes of exposure. The pesticide product is applied in irrigation water to mushrooms growing in enclosed facilities. There will not be any repeated dermal exposure to natamycin based on this application method. A review of the literature demonstrates that natamycin is not a developmental or reproductive toxicant at up to 50 mg/kg bw/day in rats and up to 15 mg/kg bw/day in rabbits.

3. *Developmental toxicity (MRID 48613501)*. In lieu of a study addressing prenatal developmental toxicity, Guideline Data Requirement (OCSPP 870.3700), the registrant developed a rationale supported with information and data obtained from the open technical literature to address the data requirement (MRID 48613501), which is available for review in the docket for this tolerance exemption. Based on the data, information, and the weight of evidence, fetal exposure from oral ingestion of natamycin in or on treated mushrooms by the mother would likely be extremely low. There are no concerns for subchronic, chronic, and reproductive/developmental toxicity resulting from

dietary exposure to natamycin-treated mushrooms. Natamycin is not a subchronic toxicant in rats when administered in the diet at up to 45 mg/kg bw/day for 96 days, nor in dogs at up to 12 mg/kg bw/day for 3 months (Refs.2, 3, and 4). Based on a lack of observable differences in tumors relative to untreated controls, natamycin is not a carcinogen in rats or dogs that were administered natamycin in the daily diet for up to 2 years (Ref. 5). The NOAEL for chronic toxicity was 22.4 mg/kg bw/day in rats and 6.25 mg/kg bw/day in dogs, based on reduced body weight. Natamycin is not a reproductive or developmental toxicant when administered to experimental animals at  $\geq 50$  mg/kg bw/day in 3-generation and 2-generation studies with rats (Ref. 6). Exposure to dietary natamycin is expected to be extremely low. Dietary natamycin is rapidly metabolized by stomach acids, poorly absorbed by mammalian systems; and its degradates are rapidly excreted in the feces within 24 hrs when orally ingested (Refs. 7, 8, and 9). Natamycin is a high molecular weight compound (666 Daltons) with low solubility in water (30-50 ppm at 20-25 °C) and many organic solvents. Chemical compounds having molecular weights >600 Daltons are not known to diffuse across the placental barrier of humans (Ref. 10) and there are no known active transport mechanisms for natamycin. Further, based on per capita consumption of all mushroom commodities in the United States (Ref. 11), dietary intake from treated, unwashed mushrooms is conservatively estimated to be no more than 0.00030 milligrams of Active ingredient per kilogram of body weight per person per day (mg a.i./kg bw/person/day) (Ref.12). This value is well below any known acute oral, subchronic and chronic dietary, reproductive, and developmental endpoints for natamycin by many orders of magnitude. Likewise, the estimated dietary intake from unwashed, treated mushrooms also is well below the Acceptable Dietary Intake (ADI) of

0.3 established by the Joint Food Agriculture Organization of the United Nations (FAO) and the World health Organization Expert Committee on Food Additives (JECFA, 2001& 2006) and an ADI of 0.1 established by the European Food Safety Authority (Ref. 13).

4. *Other.* Natamycin has a non-toxic mode of action and functions as a fungistat, preventing the germination of fungal spores. It has no effects on fungal mycelia.

Development of antibiotic resistance to natamycin has not been reported during its entire history of use.

5. *Residue analytical method (MRID 48105407).* The registrant developed and validated a residue analytical method to determine residues of natamycin in mushrooms, mushroom compost, casing, and casing plus inoculum. Samples were extracted in methanol, filtered, and then analyzed by liquid chromatography with mass spectrometry/mass spectrometry detection (LC-MS/MS). The analyte was quantified by comparison with external calibration curve using natamycin (88.7% purity). The analytes in mushroom samples and casing plus inoculum samples were quantified using a solvent-based reference standard (88.7% natamycin), whereas the analytes in compost and casing was quantified relative to a matrix-based reference standard. Samples were fortified with 0.1 or 1.0 mg/kg natamycin. Recovery for mushrooms was  $89 \pm 11\%$ . Overall recovery for compost was  $84 \pm 12\%$ , and for casing was  $99 \pm 16\%$ . Overall recovery for casing plus inoculum was  $66 \pm 8\%$ . The limit of quantitation (LOQ) was 0.01 mg/kg (ppm) for mushrooms and 0.1 mg/kg for the other matrices. There were no interfering substances. The limit of detection (LOD) was 0.25 nanograms/milliliter (ng/mL) for the reference substances. A copy of the submitted Residue Analytical Method (MRID 48105407) is available for review in the docket for this tolerance exemption.

#### **IV. Aggregate Exposures**

In examining aggregate exposure, section 408 of FFDCFA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

##### *A. Dietary Exposure*

1. *Food exposure.* Natamycin is a fungistat that has a long history of use in food for the prevention of spoilage. In evaluating exposure to natamycin, EPA considered exposure under the submitted tolerance petition for an exemption from the requirement of a tolerance for natamycin when used to control mold spores and fungi in or on mushrooms produced in an enclosed mushroom production facility. EPA assessed dietary exposure from data and information submitted by the petitioner, as well as publically available literature which demonstrates that dietary exposure from the use of natamycin as a fungistat on mushrooms produced in an enclosed mushroom production facility is expected to be minimal. Based on laboratory testing of the Technical Grade Active Ingredient (described below), and the anticipated minimal dietary exposure, and the mode of action of natamycin as a fungistat, acute and chronic dietary risks for sensitive subpopulations are not anticipated.

The active ingredient is minimally toxic (10.34% of the EP by weight), as demonstrated by Tier I Guideline toxicity studies. Finally, in connection with the proposed use of natamycin as a biopesticide intended solely for use in enclosed mushroom production facilities, all compost and casing used in mushroom production

will be autoclaved prior to being removed from the mushroom growing facilities to destroy any natamycin residues, thus preventing them from entering the outdoor environment. Based on the mode of action of the active ingredient as a fungistat, no aggregate exposure is anticipated.

2. *Drinking water exposure.* Based on the intended use sites (enclosed mushroom production facilities) and use directions (steam sterilization of compost and casing prior to disposal outside of the mushroom growth facility), it is highly unlikely that residues of natamycin will enter any sources of drinking water. However, in the unlikely event that natamycin residues escape from its indoor application site (completely enclosed mushroom houses), its concentration in surface waters would never exceed 30-50 ppm due to its low solubility in water; up to 50 ppm @ 20-25°C and pH 5-7.5; and at <pH2 or >pH 10 it completely degrades (Ref. 14). Natamycin is extremely sensitive to UV light and is completely degraded by UV within 24 hours of exposure in aqueous solution (Ref. 15). Even assuming that no environmental degradation takes place, gastric juices typically found in the human stomach will completely degrade natamycin within 24 hrs (Ref. 16). Finally, the non-definitive endpoints for acute oral toxicity (>1820 ppm) (Ref. 17) and subchronic oral toxicity (>500 ppm in the diet) (Ref. 18), are approximately 36X and 10X greater than the highest measured solubility of natamycin in water. For these reasons, the Agency believes that there are no concerns for exposure of humans to natamycin in drinking water.

## **V. Cumulative Effects from Substances with a Common Mechanism of Toxicity**

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide’s residues and “other substances that have a common mechanism of toxicity.”

EPA has not found natamycin to share a common mechanism of toxicity with any other substances, and natamycin does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that natamycin does not have a common mechanism of toxicity with other substances. For information regarding EPA’s efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA’s website at <http://www.epa.gov/pesticides/cumulative>.

## **VI. Determination of Safety for U.S. Population, Infants and Children**

FFDCA section 408(b)(2)(C) provides that EPA shall assess the available information about consumption patterns among infants and children, special susceptibility of infants and children to pesticide chemical residues and the cumulative effects on infants and children of the residues and other substances with a common mechanism of toxicity. In addition, FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA Safety Factor. In applying this provision,

EPA either retains the default value of 10X or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

Based on the acute toxicity and pathogenicity data summarized in Unit III, EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to the residues of natamycin. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. EPA has arrived at this conclusion because the data and information available on natamycin does not demonstrate toxic, pathogenic, and/or infective potential to mammals when used as a fungistat to prevent the germination of fungal spores on mushrooms produced in enclosed mushroom production facilities. Thus, there are no threshold effects of concern and, as a result, an additional margin of exposure is not necessary.

## **VII. Other Considerations**

### *A. Analytical Enforcement Methodology*

An analytical method is not required for enforcement purposes since the Agency is establishing an exemption from the requirement of a tolerance without any numerical limitation. Nonetheless, and as discussed in more detail earlier in this final rule, an analytical method was submitted with the application to register natamycin as a new active ingredient. The Agency has reviewed the analytical method and determined it to be acceptable.

### *B. International Residue Limits*

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and

agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). The Codex Alimentarius is a joint U.N. Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has not established a MRL for natamycin.

### *C. Response to Comments*

One anonymous comment was received (EPA-HQ-OPP-2010-0685-0006) in response to the notice of filing for this action. The commenter, who focused specifically on the application of “powdered natamycin” in cheese processing plants (presumably as a preservative), expressed the concern that natamycin “is a health hazard” and further asserted that people at such plants have no real protection from inhalation or dermal exposures to powdered natamycin. In response, the Agency notes that under the FFDCA, the controlling standard governing EPA’s consideration of a petition for a tolerance exemption is whether there is a reasonable certainty that no harm will result from aggregate exposure to natamycin, including all anticipated dietary exposures and all other non-occupational exposures for which there is reliable information. Worker risk issues, therefore, are not relevant in the context of the Agency’s assessment of a petition for a tolerance exemption under the FFDCA. For all the reasons noted in this Final Rule, EPA has determined that there is a reasonable certainty that no harm will result from aggregate

exposure to residues of natamycin, including all anticipated dietary exposures and all other (non occupational) exposures for which there is reliable information. This finding is specific to natamycin residues resulting in or on mushrooms when natamycin is used as a fungistat to prevent the germination of fungal spores on mushrooms produced in mushroom production facilities. Worker risk issues, where relevant, were taken into consideration in the context of EPA's separate consideration (under FIFRA) of the applications for registration of the pesticide products containing natamycin as a new biochemical active ingredient for use on mushrooms in enclosed mushroom production facilities. Specifically, EPA reviewed, among other things, data and information (MRIDS 48105505 and 48105510) submitted specifically to address the Agency's data requirements for dermal and inhalation toxicity (OCSPP 870.1200; 870.1300, 8703250 and 870.3465). Based on that review, the Agency categorized natamycin as a toxicity IV active ingredient. Toxicity Categories are determined based on hazard indicators by considering oral, dermal, inhalation and eyes routes of exposure. A Toxicity Category IV is defined as a pesticide product that is non toxic or slightly toxic and not an irritant by all routes of and determined that natamycin, as formulated in the two products (EPA File Symbol 87485-1 and 87485-2) at issue, is reasonably not expected to cause harm when used according to product labeling. Finally, in light of the commenter's focus on powdered natamycin, it is also worth noting that the one end use product that EPA is registering does not contain powdered natamycin. Instead, it is contained in a liquid suspension formulation that is directly added to irrigation water using standard irrigation equipment. In addition, all mixers, loaders, applicators and handlers will be required through instructions on the product label to wear personal protective garments (protective

eyewear, long sleeved shirt, long pants and socks and shoes). To be clear, though, these separate registration decisions under FIFRA are not the focus of or at issue in connection with this Final Rule granting a tolerance exemption under the FFDCFA.

### **VIII. Conclusions.**

Therefore, an exemption from the requirement of a tolerance is established for residues of natamycin in or on mushrooms when used as a fungistat to prevent the germination of fungal spores on mushrooms produced in enclosed mushroom production facilities.

### **IX. References**

1. Joint FAO/WHO Expert Committee on Food Additives (JECFA). 1968, 1969, 1976, 2002, 2006, and 2007. See EFSA 2009 for specific reference citations.
2. Hutchinson, E. B., W. E. Ribelin, and G. J. Levinskas. 1966. Report on acid-degraded pimaricin: Ninety-eight day repeated feeding to rats. Unpublished report submitted to WHO by American Cyanamid Co., Central Medical Department.
3. Levinskas, G. J., W. E. Ribelin, and C. B. Shaffer. 1966. Acute and chronic toxicity of pimaricin. *Toxicology and Applied Pharmacology* 8: 97-109.
4. Van Ecken, C. J., R. D. R. Birtwhistle, and M. J. e. Aboulwafa-wan Velthoven. 1984. Three months study in dogs of the toxicity of natamycin by addition to the food. Unpublished report 12.401, 24 October 1984. Submitted to WHO by Gist-Brocades Research and Development.
5. Levinskas, G. J., C. B. Shaffer, C. Bushey, M. L. Kunde, D. W. Stackhouse, L. B. Vidone, B. Javier, and E. Monell. 1963. Two year feeding study in rats. Unpublished

report from the Central Medical department. Submitted to WHO by American Cyanamid Co.

6. Cox, G. E., D. E. Bailey, and K. Morgareidge. 1973. Multigeneration studies in rats with Delvocid brand of pimaricin. Unpublished report No. 1-1052 submitted to WHO by Food and Drug Research Laboratories, Inc.

7. Blankwater, Y. J. and W. Hespe. 1979. Autoradiographic and bioautographic study of the distribution of oral natamycin in the rat. Unpublished report No. 20.502, dated 8 May 1979 from Gist-Brocades NV, Delft.

8. Hespe, W. and A. M. Meier. 1980. Studies involving the resorption of radioactivity following the oral administration of <sup>14</sup>C-pimaricin, applied on cheese, in comparison to other oral forms of administration. Unpublished report No. 20.532, dated 4 February 1980, submitted to WHO by Gist-Brocades NV, Haarlem.

9. Morgenstern, A. P. and G. J. A. M. Muskens. 1976. Further data on the toxicity of the decomposition products of pimaricin. Unpublished report Gist-Brocades NV, Delft, 4 pages.

10. Pacifici, G. M. and R. Nottoli. 1995. Placental transfer of drugs administered to the mother. *Clinical Pharmacokinetics* 28(3)

11. USDA/ERS. 2010. Mushrooms: Supply and Utilization and Per Capita Consumption. February 2010 Update.

[www.ers.usda.gov/data/foodconsumption/spreadsheets/mushroom.xls](http://www.ers.usda.gov/data/foodconsumption/spreadsheets/mushroom.xls) (Accessed 04/04/2011).

12. USEPA 2011. Memorandum from R.S. Jones to C Greene, dated 04/11/2011

13. European Food Safety Authority (EFSA). 2009. Scientific opinion on the use of natamycin (E 235) as a food additive. EFSA Panel of Food Additives and Nutrient Sources added to Food (ANS). EFSA Journal 7(12):1412, 25 p.

<http://www.efsa.europa.eu/en/efsajournal/doc/1412.pdf> (Accessed 04/04/2011)

14. USEPA. 2011. Science Review in Support of the Registration of natamycin TGAI, a Technical Grade Active Ingredient (TGAI) Product; and Natamycin L, an End-Use Product (EP), Respectively Containing 91.02% and 10.34% natamycin, a New Active Ingredient. Hazard Assessment for Tier I Toxicity Studies and Waiver Requests, Tier I Non-Target Organism Waiver Requests, and Metabolism/Residue Studies. Memorandum from R. S. Jones to C. Greene, dated 04/04/2011.

15. Joint FAO/WHO Expert Committee on Food Additives (JECFA). 2006. Summary and Conclusions. Sixty-Seventh Meeting. Rome, 20-29 June 2006.

[ftp://ftp.fao.org/ag/agn/jecfa/jecfa67\\_final.pdf](ftp://ftp.fao.org/ag/agn/jecfa/jecfa67_final.pdf) (Accessed 04/04/2011)

16. Koontz, J. L., J. E. Marcy, W. E. Barbeau, and S. E. Duncan. 2003. Stability of Natamycin and Its Cyclodextrin Inclusion Complexes in Aqueous Solution. *Journal of Agricultural Food Chemistry*. 51 (24): 7111–7114

17. USEPA. 2011. Science Review in Support of the Registration of Natamycin TGAI, a Technical Grade Active Ingredient (TGAI) Product; and Natamycin L, an End-Use Product (EP), Respectively Containing 91.02% and 10.34% Natamycin, a New Active Ingredient. Hazard Assessment for Tier I Toxicity Studies and Waiver Requests, Tier I Non-Target Organism Waiver Requests, and Metabolism/Residue Studies. Memorandum from R. S. Jones to C. Greene, dated 04/04/2011.

18. Subchronic (rat) feeding studies demonstrate that the No Observable Adverse Effect Level NOAEL was 500 ppm in the diet (42 mg/kg bw/day for males and 48 mg/kg bw/day for females) (MRID 48105511).

#### **X. Statutory and Executive Order Reviews**

This final rule establishes a tolerance exemption under section 408(d) of FFDCA in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993). Because this final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, nor does it require any special considerations under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under section 408(d) of FFDCA, such as the tolerance exemption in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*) do not apply.

This final rule directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of section 408(n)(4) of FFDCA. As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled Federalism (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled Consultation and Coordination with Indian Tribal Governments (65 FR 67249, November 9, 2000) do not apply to this final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Public Law 104-4).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104-113, section 12(d) (15 U.S.C. 272 note).

#### **XI. Congressional Review Act**

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, generally provides that before a rule may take effect, the agency promulgating the rule must submit a rule report to each House of the Congress and to the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U.S.

Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of this final rule in the **Federal Register**. This final rule is not a “major rule” as defined by 5 U.S.C. 804(2).

**List of Subjects in 40 CFR Part 180**

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: May 8, 2012.

**Steven Bradbury,**

*Director, Office of Pesticide Programs.*

Therefore, 40 CFR chapter I is amended as follows:

**PART 180--[AMENDED]**

1. The authority citation for part 180 continues to read as follows:

**Authority:** 21 U.S.C. 321(q), 346a and 371.

2. Section 180.1315 is added to subpart D to read as follows:

**§180.1315 Natamycin; exemption from the requirement of a tolerance.**

An exemption from the requirement of a tolerance is established for residues of natamycin in or on mushrooms when applied as a fungistat to prevent the germination of fungal spores on mushrooms produced in enclosed mushroom production facilities.