BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Candida oleophila Strain O

PC Code: 021010

U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division

Last Updated – July 15, 2009

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I. EXECUTIVE SUMMARY

Candida oleophila Strain O is a single-celled yeast found naturally on plant tissues (fruits, flowers, and wood) and in water. It was originally isolated from golden delicious apples and is intended for use as an antagonist to control the fungal pathogens, gray mold (*Botrytis cinerea*) and blue mold (*Penicillium expansum*), which cause post-harvest decay on apples and pears. The mode of action for *Candida oleophila* Strain O is primarily through competition for nutrients and pre-colonization of plant wound sites (Jijakli *et al*. 1993), although information provided to the Agency suggests that production of beta-1,3-glucanases (i.e., hydrolytic enzymes that can degrade fungal phytopathogen cell walls) may also contribute to its antagonistic activity.

To decide whether to grant a unconditional registration under Section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to NEXY, a proposed end-use product containing *Candida oleophila* Strain O as an active ingredient at 57.0% by weight, the Biopesticides and Pollution Prevention Division (BPPD) reviewed microbial pesticide product chemistry and composition, analysis and certified limits, physical and chemical characteristics, mammalian and non-target organism toxicology, and environmental fate data [40 Code of Federal Regulations (CFR) §§ 158.2120, 158.2140, and 158.2150]. It was determined that the data/information submitted adequately satisfy current data requirements.

Adequate mammalian toxicology data/information were submitted to support the registration of NEXY. Acceptable acute toxicity guideline studies were submitted, and data waivers were granted by the Agency to fulfill the remaining Tier I acute toxicity data requirements based on the lack of toxicity, infectivity, and/or pathogenicity of *Candida oleophila* Strain O, as well as the nature of the inert ingredients in the NEXY formulation. Additionally, two mutagenicity studies not required for the registration of this active ingredient were voluntary submitted by the registrant and indicated that *Candida oleophila* Strain O did not have mutagenic potential.

Although dietary exposure to *Candida oleophila* Strain O may occur through consumption of treated apples and pears, the following factors were considered by the Agency in making its decision to register this microbial pesticide: (1) lack of acute oral toxicity/pathogenicity, (2) inability of *Candida oleophila* Strain O to grow at mammalian body temperatures, (3) absence of clinical reports of infections despite the common occurrence of *Candida oleophila* on various food commodities consumed by the United States population, (4) standard practices for processing fruit (i.e., washing, peeling, and cooking), which would reduce residues of *Candida oleophila* Strain O several orders of magnitude below the dose tested in the acute oral toxicity/pathogenicity study, and (5) prior establishment of an exemption from the requirement of a tolerance for residues of a similar strain of yeast, *Candida oleophila* isolate I-182, when used as a post-harvest biological fungicide in or on all raw agricultural commodities (40 CFR § 180.1144). Furthermore, drinking water and non-dietary, non-occupational exposures to *Candida oleophila* Strain O are unlikely to occur because of the proposed use pattern, use sites, and application methods specified on NEXY's product label. Cumulative effects are not

anticipated because *Candida oleophila* Strain O has no demonstrated toxicity. The Environmental Protection Agency (EPA) concluded that the data submitted for the NEXY registration meet the safety requirements of the Food Quality Protection Act (FQPA) of 1996, and support an exemption from the requirement of a tolerance for the residues of *Candida oleophila* Strain O on apples and pears. If the microbial active ingredient is used in accordance with the product label, there is a reasonable certainty that no harm will result from aggregate exposure to the United States population, including infants and children, to the residues of *Candida oleophila* Strain O. As a result of this determination, EPA established a permanent exemption from the requirement of a tolerance for residues of the microbial pesticide, *Candida oleophila* Strain O, on apples and pears when applied/used as a post-harvest biofungicide (40 CFR § 180.1289).

Personal protective equipment (PPE) is required for mixers, loaders, and applicators that may be exposed for prolonged periods to *Candida oleophila* Strain O due to their occupation. Mixers and loaders must wear a dust/mist filtering respirator meeting National Institute for Occupational Safety and Health (NIOSH) standards of at least N-95, R-95, or P-95 because of an incident in which three workers reported clinical symptoms of a respiratory reaction after being exposed to large amounts of *Candida oleophila* Strain O and wearing no PPE. No adverse dermal effects have been reported. Nevertheless, the Agency believes that the potential for dermal hypersensitivity incidents is best mitigated by label requirements that a long-sleeved shirt, long pants, socks, shoes, and waterproof gloves be worn when mixing, loading, or applying the product, or when handling crates containing treated apples and pears. Protective eyewear is also required when mixing, loading, or applying the product or when handling crates containing treated apples and pears, based upon the results of the submitted acute eye irritation study.

Adequate non-target toxicology data/information are available to support registration of NEXY, which contains *Candida oleophila* Strain O, for intended indoor uses on pome fruits (pears, apples). Because of these intended uses, direct exposures to most terrestrial and all aquatic environments are not expected, and therefore, all non-target toxicology data requirements for *Candida oleophila* Strain O were satisfied with appropriate data waiver requests and rationales. No risks to non-target organisms (to include federally listed endangered and threatened species) or to the environment are anticipated as a result of the intended indoor uses of *Candida oleophila* Strain O. If future uses include outdoor uses where exposures of non-target organisms would be increased, additional data and/or information must be submitted to and reviewed by the EPA.

II. ACTIVE INGREDIENT OVERVIEW

Biological Name:	*Candida oleophila* Strain O
Culture Deposit:	Belgian Coordinated Collections of Microorganisms (BCCM)/Mycothèque de l'Université Catholique de Louvain (MUCL) in Louvain-la-Neuve, Belgium under Accession Number MUCL 40564
Office of Pesticide Programs (OPP) Chemical Code:	021010
Type of Pesticide:	Microbial Pesticide – Post-Harvest Biofungicide See Appendix B for specific information (i.e., use sites, application rate, method of application, formulation type, and target pests) regarding the end-use product, NEXY, containing this active ingredient.

III. REGULATORY BACKGROUND

On December 28, 2007, SynTech Global, LLC (address: P.O. Box 640, Hockessin, Delaware 19707), acting as the United States authorized agent for BioNext sprl (address: Passage des déportés, 2, B-5030 Gembloux, Belgium), submitted an application to register NEXY (EPA File Symbol 84863-R) under Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act. On March 28, 2008, the EPA announced receipt of this application to register a pesticide product containing a new active ingredient [73 Federal Register (FR) 16676] and opened a 60-day public comment period.

One comment was received in response to the notice of receipt. A private citizen expressed opposition to *Candida oleophila* Strain O's introduction into the United States in light of the "thousands of chemicals already out there" and implied a concern about the effects of "toxic chemicals" on human health and the environment. Pursuant to its authority under FIFRA, the Agency conducted a rigorous assessment of *Candida oleophila* Strain (as described throughout this document) and concluded that it is not expected to cause any unreasonable adverse effects to human health or the environment. Further, *Candida oleophila* Strain O is not considered a conventional pesticide. Conventional pesticides generally consist of synthetic materials, may affect a broad spectrum of non-target organisms, and may be inherently more toxic. *Candida oleophila* Strain O, however, is a naturally occurring yeast isolated from golden delicious apples and found on various food commodities, and has been classified as a microbial pesticide. *Candida oleophila* Strain O is intended for use as an antagonist to specifically control the fungal pathogens, gray mold (*Botrytis cinerea*) and blue mold (*Penicillium expansum*),

which cause post-harvest decay on apples and pears. The mode of action for *Candida oleophila* Strain O is primarily through competition for nutrients and pre-colonization of plant wound sites, and use of *Candida oleophila* Strain O may result in decreased conventional pesticide applications to apples and pears after harvest.

Concurrent with their registration application, and under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996, SynTech Global, LLC submitted a petition to establish an exemption from the requirement of a tolerance for *Candida oleophila* Strain O [Pesticide Petition (PP) 7F7310]. In the Federal Register dated March 28, 2008 (73 FR 16673), the EPA announced that SynTech Global, LLC proposed to establish an exemption from the requirement of a tolerance for residues of the microbial pesticide, *Candida oleophila* Strain O, on apples and pears when used as a post-harvest biofungicide and opened a 30-day public comment period. No comments were received following this publication.

On May 13, 2009, the Agency established a permanent exemption from the requirement of a tolerance for residues of the microbial pesticide, *Candida oleophila* Strain O, on apples and pears when applied/used as a post-harvest biofungicide (40 CFR § 180.1289; 74 FR 22460]. Shortly thereafter and pursuant to FIFRA section 3(c)(5), an unconditional registration was issued for NEXY on June 1, 2009 (EPA Registration Number 84863-1).

IV. RISK ASSESSMENT

On October 26, 2007, the Agency issued a Final Rule in the Federal Register on the data requirements to support registration of biochemical and microbial pesticides, and updated the definitions for biochemical and microbial pesticides (72 FR 61002). The rule became effective on December 26, 2007. The data and information evaluated for this Biopesticides Registration Action Document (BRAD) were considered in light of these requirements.

The classifications that are found for each data submission are assigned by EPA science reviewers and are an indication of the usefulness of the information contained in the documents for risk assessment. A rating of "ACCEPTABLE" indicates the study is scientifically sound and is useful for risk assessment. A "SUPPLEMENTAL" rating indicates the data provide some information that can be useful for risk assessment. The studies may have certain aspects determined not to be scientifically acceptable ("SUPPLEMENTAL: UPGRADABLE"). If a study is rated as "SUPPLEMENTAL: UPGRADABLE," the Environmental Protection Agency always provides an indication of what is lacking or what can be provided to change the rating to "ACCEPTABLE." If there is simply a "SUPPLEMENTAL" rating, the reviewer will often state that the study is not required by the current 40 CFR Part 158. Both "ACCEPTABLE" and "SUPPLEMENTAL" studies may be used in the risk assessment process as appropriate. An "UNACCEPTABLE" rating indicates that new data need to be submitted.

For product-specific acute toxicity data requirements, toxicity categories are assigned

based on the hazard(s) identified from studies and/or information submitted to the Agency. The product is classified into Toxicity Category I, II, III, or IV, where Toxicity Category I indicates the highest toxicity and Toxicity Category IV indicates the lowest toxicity.

A. Product Analysis Assessment (40 CFR § 158.2120)

All product analysis data requirements for Section 3(c)(5) registration of NEXY, containing *Candida oleophila* Strain O as an active ingredient, have been satisfied by either acceptable guideline studies or waiver rationales. For a comprehensive guideline-by-guideline summary of the product analysis data requirements described in sections IV(A)(1), IV(A)(2), and IV(A)(3), refer to Table 1 in Appendix A.

1. Product Chemistry and Composition [Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Guidelines 885.1100, 885.1200, and 885.1300]

Candida oleophila Strain O is a single-celled yeast [approximately 1 micrometer (µm) in diameter] in the phylum Ascomycota, the class Ascomycetes, and the family Saccharomycetaceae. Found naturally on plant tissues (fruits, flowers, and wood) and in water, it was originally isolated from golden delicious apples. *Candida oleophila* Strain O reproduces asexually by budding. After 3 days at 25°C, a few cells are spheroidal but most are ovoidal or long-ovoidal to elongate. The cells occur singly, in pairs, and in short-branched and unbranched chains. No production of antibiotics or toxic volatile compounds has been observed. According to reported testing, *Candida oleophila* Strain O does not grow above 33 °C, is sensitive to ultraviolet light, and is dependent on a carbon source for growth (Jijakli *et al*. 1993). Some species of *Candida*, namely *Candida albicans* and *Candida glabrata*, have been found as opportunistic pathogens to humans (mainly the immunosuppressed) and/or animals (Yemma and Berk 1994). *Candida oleophila*, however, is an environmental microbe unable to grow at mammalian body temperatures and is easily distinguished from the *Candida* species reported as clinical isolates. More importantly, no pathogenic effects or infections from *Candida oleophila* Strain O were seen in the submitted infectivity studies as described in section IV(B)(1)(a). *Candida oleophila* has not been reported to produce toxins against plants or animals, and no production of toxins has been observed under laboratory conditions.

Candida oleophila Strain O is intended for use as an antagonist to control the fungal pathogens, gray mold (*Botrytis cinerea*) and blue mold (*Penicillium expansum*), that cause post-harvest decay on apples and pears. The mode of action for *Candida oleophila* Strain O is primarily through competition for nutrients and pre-colonization of plant wound sites (Jijakli *et al*. 1993). Submitted data also suggest that production of beta-1,3-glucanases (i.e., hydrolytic enzymes that can degrade fungal phytopathogen cell walls) may contribute to its antagonistic activity.

Submitted data also adequately describe the production process, potential microbial contaminants, and potential carryover impurities from the inert ingredients; therefore, the

requirements for manufacturing process and discussion of formation of unintentional ingredients have been satisfied.

2. Analysis and Certified Limits (OPPTS Guidelines 885.1400 and 885.1500)

Results of a five-batch preliminary analysis were provided and the requirement for analysis of samples has been satisfied.

The certified limits for the active and inert ingredients exceed the OPPTS Guideline 830.1750 specified ranges, but an acceptable explanation was provided; therefore, the requirement for certified limits has been satisfied.

3. Physical and Chemical Characteristics (OPPTS Guidelines 830.6302, 830.6303, 830.6304, 830.6313, 830.6317, 830.6319, 830.6320, 830.7000, 830.7100, and 830.7300)

Submitted data adequately describe the physical and chemical characteristics and waiver rationales provided are acceptable; therefore, the requirements for color, physical state, odor, stability to normal and elevated temperatures, metals, and metal ions, storage stability, miscibility, corrosion characteristics, pH, viscosity, and density/relative density/bulk density (specific gravity) have been satisfied.

B. Human Health Assessment

1. Toxicology

Adequate mammalian toxicology data/information are available to support the registration of NEXY, which contains *Candida oleophila* Strain O. All Tier I toxicology data requirements for *Candida oleophila* Strain O and its associated end-use product have been satisfied by guideline studies or waiver rationales. Tier II and Tier III studies were not required for *Candida oleophila* Strain O based on the lack of acute toxicity/pathogenicity in the Tier I studies. Two mutagenicity studies were submitted and reviewed, although they were not required for *Candida oleophila* Strain O.

For a comprehensive guideline-by-guideline summary of the toxicology data requirements and additional studies described in sections IV(B)(1)(a), IV(B)(1)(b), and IV(B)(1)(c), refer to Table 2 and Table 3 in Appendix A.

a. Acute Toxicity/Pathogenicity – Tier I (40 CFR § 158.2140)

Acute Oral Toxicity and Pathogenicity – Rat [OPPTS Guideline 885.3050; Master Record Identification (MRID) Number (No.) 473138-07]: In an acute oral toxicity and pathogenicity study, groups of rats were given a single oral dose of *Candida oleophila* Strain O at a dose of 2.3–3.8 x 10^8 colony-forming units (cfu)/animal. The animals were observed for a period of up to 22 days with interim scheduled sacrifices on days 4, 8, and 15. There were no treatment-related clinical signs, necropsy findings, or changes in body

weight. No test organisms were recovered from the gastrointestinal contents, any organs, or blood of any animal or feces from treated animals sacrificed on day 22. Based on the results of this study, *Candida oleophila* Strain O does not appear to be toxic, infective, and/or pathogenic in rats. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Pulmonary Toxicity and Pathogenicity – Rat (OPPTS Guideline 885.3150; MRID No. 473138-09): In an acute pulmonary toxicity and pathogenicity study, groups of rats were exposed by the intratracheal route to *Candida oleophila* Strain O at a dose of 1.2–5.2 x 10^8 cfu/animal. The animals were observed for up to 22 days. There were no test substance-related clinical signs, necropsy findings, or changes in body weight. Test organisms were recovered in the lungs from the treated males and females sacrificed one hour post dosing with clearances by day 4. No test organisms were recovered from the gastrointestinal contents, organs, or blood of any animal or feces from treated animals sacrificed on day 22. Based on these results, *Candida oleophila* Strain O does not appear to be toxic, infective, and/or pathogenic to rats at 1.2–5.2 x 10^8 cfu/animal. This study was rated "ACCEPTABLE" for risk assessment purposes.

Acute Subcutaneous Injection Toxicity and Pathogenicity – Rat (OPPTS Guideline 885.3200; MRID No. 473138-08): In an acute subcutaneous injection toxicity and pathogenicity study, groups of rats were injected subcutaneously with *Candida oleophila* Strain O with a dose of 1.1–2.0 x 10^7 cfu/animal. The animals were observed for up to 22 days. There were no treatment-related clinical signs, necropsy findings, or changes in body weight. No test organisms were recovered from the gastrointestinal contents, organs, blood, or the injection site of any animal. Based on the results of this study, *Candida oleophila* Strain O does not appear to be toxic, infective, and/or pathogenic in rats when dosed at 1.1–2.0 x 10^7 cfu/animal. This study was rated "ACCEPTABLE" for risk assessment purposes.

Hypersensitivity Incidents (OPPTS Guideline 885.3400; MRID No. 473138-12): During a pilot-plant production trial of NEXY using fermentation vessels and involving large amounts of *Candida oleophila* Strain O, three of six workers (all on the same work team) not wearing personal protective equipment reported clinical symptoms of a respiratory reaction. As a result, the product label requires that mixers and loaders wear a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95, or P-95, which will also be worn by workers in the production facility. Due to the application methods (dipping and drenching), respiratory exposure to operators during pesticide application is not anticipated. No adverse dermal effects have been reported by workers, and dermal sensitization to operators or consumers is not anticipated. Nevertheless, potential for dermal hypersensitivity incidents has been mitigated by label requirements that a long-sleeved shirt, long pants, socks, shoes, and waterproof gloves be worn when mixing, loading, or applying the product or when handling crates containing treated apples and pears. Any future hypersensitivity incidents must be reported per OPPTS Guideline 885.3400.

Cell Culture (OPPTS Guideline 885.3500): This study is not required because *Candida oleophila* Strain O is not a virus (refer to test note #4 of 40 CFR § 158.2140(d)).

Acute Oral Toxicity (OPPTS Guideline 870.1100; MRID No. 475610-01): Waived based on the results of MRID No. 473138-07, which showed that *Candida oleophila* Strain O was not toxic, infective, and/or pathogenic via oral route of exposure, and the nature of the inert ingredients in NEXY's formulation. This waiver request was rated "ACCEPTABLE" and NEXY was classified as TOXICITY CATEGORY IV.

Acute Dermal Toxicity (OPPTS Guideline 870.1200; MRID No. 473227-01): Waived based on the results of MRID No. 473138-08 (which showed that *Candida oleophila* Strain O was not toxic, infective, and/or pathogenic via subcutaneous route of exposure), MRID No. 473138-11 (which showed that NEXY was not irritating to the skin of rabbits at a dose of 0.5 gram/animal), and the nature of the inert ingredients in NEXY's formulation. This waiver request was rated as "ACCEPTABLE" and NEXY was classified as TOXICITY CATEGORY III.

Acute Inhalation Toxicity (OPPTS Guideline 870.1300; MRID No. 475610-01): Waived based on the results of MRID No. 473138-09, which showed that *Candida oleophila* Strain O was not toxic, infective, and/or pathogenic via pulmonary route of exposure, and the nature of the inert ingredients in NEXY's formulation. This waiver request was rated "ACCEPTABLE" and NEXY was classified as TOXICITY CATEGORY III.

Acute Eye Irritation – Rabbit (OPPTS Guideline 870.2400; MRID No. 473138-10): In an acute eye irritation study, 100 milligrams (mg) of NEXY was instilled into the conjunctival sac of the right eye of four rabbits. Thirty seconds after treatment, the eye of the first rabbit was rinsed with saline. Animals were observed for 15 days. Irritation was scored and classified by the system of Kay and Calandra. No corneal opacity or iritis was noted on the unwashed eyes of three rabbits. Positive conjunctival irritation was noted on 1 of 3 rabbits 24 hours after test material instillation, with reduction to score 1 by 48 through 72 hours, and with clearance by day 8. In this study, NEXY was minimally irritating to the eye based on the highest maximum mean total score of 6.7, recorded 1 hour after test material instillation. This study was rated "ACCEPTABLE" for risk assessment purposes and NEXY was classified as TOXICITY CATEGORY III for acute eye irritation by dose of 100 mg per animal.

Primary Dermal Irritation – Rabbit (OPPTS Guideline 870.2500; MRID No. 473138-11): In a primary dermal irritation study, three rabbits were dermally exposed to 0.5 grams (g) of NEXY for 4 hours to a 25 millimeter (mm) x 25 mm area of body surface. The animals were observed for 72 hours. Irritation was scored by the method of Draize. No dermal irritation was noted on any rabbit during the study. The Primary Irritation Index (PII) was 0.0, the study was rated "ACCEPTABLE" for risk assessment purposes, and NEXY was classified as TOXICITY CATEGORY IV for primary dermal irritation by dose of 0.5 g per animal.

b. Acute Toxicology and Subchronic Toxicity/Pathogenicity – Tier II; Reproductive Fertility Effects, Carcinogenicity, Immunotoxicity, and Infectivity/Pathogenicity Analysis – Tier III (40 CFR § 158.2140)

Tier II and Tier III studies were not required for *Candida oleophila* Strain O based on the lack of acute toxicity/pathogenicity in the Tier I studies.

c. Additional Studies

Additional studies, which are not included in the current microbial pesticide toxicology data requirements and are not required for *Candida oleophila* Strain O, were submitted to the Agency. These studies are as follows:

Bacterial Reverse Mutation Test (OPPTS Guideline 870.5100; MRID No. 473138-13) and In vitro Mammalian Cell Gene Mutation Test (OPPTS Guideline 870.5300; MRID No. 473138-14): Two mutagenicity studies were reviewed and indicated that *Candida oleophila* Strain O did not have mutagenic potential. These studies were rated "SUPPLEMENTAL" for the purposes of risk assessment and are not required for *Candida oleophila* Strain O.

d. Effects on the Endocrine System

Section 408(p) of the Federal Food, Drug, and Cosmetic Act (FFDCA) requires EPA to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of its program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. The Environmental Protection Agency also adopted EDSTAC's recommendation that the Program include evaluations of potential effects on wildlife.

The Agency has no knowledge of *Candida oleophila* Strain O being an endocrine disruptor, nor is this microbe related to any class of known endocrine disruptors. Following several routes of exposure in rodents, the Tier I toxicology data (see section IV(B)(1)(a)) indicated that the immune system was still intact and able to process and clear *Candida oleophila* Strain O from a variety of organs and tissues. Additional data, specifically on the endocrine effects of this microbial pesticide, are not required at this time. When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disruptor Screening Program (EDSP) have been developed and vetted, *Candida oleophila* Strain O may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

2. Dietary Exposure and Risk Characterization

Dietary exposure to *Candida oleophila* Strain O is likely to occur, mainly through food. *Candida oleophila* Strain O is naturally present on apples as it was originally isolated in 1991 from the surface of golden delicious apples. Based on information submitted to the Agency, population densities of white yeasts are estimated to reach 1.5×10^3 cfu/square centimeter (cm^2) on harvested apples, which includes the natural population of *Candida oleophila*. Background levels of *Candida oleophila* Strain O on apples are expected to be below 1.5×10^3 cfu/cm^2. Post-harvest treatment with *Candida oleophila* Strain O will probably lead to a temporary increased level of this yeast on apples. The mode of action of *Candida oleophila* Strain O is primarily based on competition for nutrients; therefore, sufficient colonization of apple surfaces has to be reached to ensure efficacy of the active ingredient. The recommended application rate of *Candida oleophila* Strain O leads to an expected residual *Candida oleophila* Strain O population of approximately 4×10^4 cfu/cm^2 (10^5 cfu/apple). Standard practices of washing, peeling, cooking, or processing fruits further reduces residues of *Candida oleophila* Strain O and minimizes dietary exposure. Actual dietary exposure is expected to be several orders of magnitude lower than the dose used in the acute oral toxicity/pathogenicity test described in section IV(B)(1)(a), during which no toxic or pathogenic effects were observed in rats.

Additionally, *Candida oleophila* Strain O has exhibited no ability to grow at mammalian body temperatures (see section IV(A)(1)), there have been no clinical reports of infections despite the ubiquitous nature of *Candida oleophila* on various food commodities (e.g., olives, apples, strawberries, fermenting grapes, and tomatoes) consumed by the United States population, and an exemption from the requirement of a tolerance for residues of *Candida oleophila* isolate I-182, which is a similar active ingredient when compared to *Candida oleophila* Strain O, was previously established by the Agency for post-harvest biofungicide use in or on all raw agricultural commodities (40 CFR § 180.1144).

Based on all of the considerations as outlined above, the Agency concludes that there is a reasonable certainty that no harm will result from the aggregate exposure to the residues of *Candida oleophila* Strain O in food.

3. Drinking Water Exposure and Risk Characterization

Exposure of humans to residues of *Candida oleophila* Strain O in drinking water is unlikely. The use pattern, use sites, and application methods for *Candida oleophila* Strain O (i.e., indoor dip or drench application to apples and pears after harvest and prior to storage) does not include direct application to aquatic environments. In the unlikely event that *Candida oleophila* Strain O was transferred to surface or ground water intended for eventual human consumption, the microbe would not survive the conditions water is subjected to in a drinking water treatment facility, including flocculation, chlorination, pH adjustments, and/or filtration. Even if oral exposure should occur through drinking water, the Agency concludes that there is a reasonable certainty that no harm will result from the exposure to the residues of *Candida oleophila* Strain O in all the anticipated

drinking water exposures because of the lack of acute oral toxicity/pathogenicity to mammals (see section IV(B)(1)(a)) and the ubiquitous nature of the microbe.

4. Acute and Chronic Dietary Exposure and Risks for Sensitive Subpopulations, Particularly Infants and Children

Section 408(b)(2)(C) of the FFDCA 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) also provides that EPA shall apply an additional tenfold 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 unless EPA determines that a different margin of safety will be safe for infants and children. Margins of exposure (safety), which are often referred to as uncertainty factors, are incorporated into EPA risk assessment either directly or through the use of a margin of exposure analysis, or by using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk.

Based on the acute toxicity and pathogenicity data discussed in section IV(B)(1)(a), the Environmental Protection Agency concludes that there is a reasonable certainty that no harm to sensitive subpopulations, including infants, children, and adults, will result from the use of *Candida oleophila* Strain O in the end-use product, NEXY. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. The Agency has arrived at this conclusion because the data available on *Candida oleophila* Strain O do not demonstrate toxic, pathogenic, or infective potential to mammals. Thus, there are no threshold effects of concern and, as a result, the provision requiring an additional margin of safety does not apply. Further, the considerations of consumption patterns, special susceptibility, and cumulative effects do not apply to pesticides without a demonstrated significant adverse effect.

5. Occupational, Residential, School, and Daycare Exposure and Risk Characterization

Significant additional human exposure to *Candida oleophila* Strain O from its pesticidal use is not expected in occupational, residential, school, or daycare areas.

a. Occupational Exposure and Risk Characterization

Even though a report was submitted to the Agency indicating that three workers exhibited clinical symptoms of a respiratory reaction, potential worker and handler exposure to *Candida oleophila* Strain O is not expected to pose any undue risk if the end-use product is used as labeled. As explained in section IV(B)(1)(a), the three workers were exposed to large amounts of *Candida oleophila* Strain O during a pilot-plant production trial of NEXY using fermentation vessels and were not wearing any personal protective equipment. To mitigate the possibility for occupational exposure to *Candida oleophila* Strain O and potential for respiratory allergic sensitization, mixers and loaders working

with NEXY must wear a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95, or P-95. Furthermore, although no adverse dermal effects have been reported by workers and dermal sensitization to operators is not anticipated, potential for dermal hypersensitivity incidents is mitigated by label requirements that a long-sleeved shirt, long pants, socks, shoes, and waterproof gloves be worn when mixing, loading, or applying the product or when handling crates containing treated apples and pears. Lastly, protective eyewear is also required when mixing, loading, or applying the product or when handling crates containing treated apples and pears because of exposure potential and the results of the acute eye irritation study.

b. Residential, School, and Daycare Exposure and Risk Characterization

According to the label, NEXY is to be applied to pears and apples after harvest and before storage, which is a distinct agricultural use. No indoor residential, school, or daycare uses currently appear on the label; thus, human exposure to *Candida oleophila* Strain O should not occur in these areas.

6. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation

In examining aggregate exposure, Section 408 of the FFDCA 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).

Potential non-occupational dermal or inhalation exposure is considered unlikely for this distinctly agricultural use (i.e., post-harvest treatment of the harvested portions—pears and apples—of agricultural plants). Oral exposure, via food and drinking water, was described in section IV(B)(2) and section IV(B)(3), respectively. While a general residential, school, and daycare exposure and risk characterization is provided in section IV(B)(5)(b), additional discussion of non-occupational dermal and inhalation exposures are found below.

a. Dermal Exposure

Non-occupational dermal exposure to *Candida oleophila* Strain O, when used as labeled, is expected to be negligible because it is limited to post-harvest agricultural treatment of apples and pears. However, should non-occupational dermal exposure occur through treated food commodities, the risk posed by this low toxicity microbe is likely to be minimal based on the toxicity and pathogenicity tests described in section IV(B)(1)(a). Furthermore, exposure would not be expected to exceed background as similar yeasts and those in the genus and species, *Candida oleophila*, are commonly associated with particular food commodities.

b. Inhalation exposure

Non-occupational inhalation exposure to *Candida oleophila* Strain O, when used as labeled, is expected to be negligible because of the method of application (i.e., dipping and drenching of apples and pears), which then allows sufficient time for drying prior to distribution to consumers. Furthermore, most of the residual yeast on apples and pears is trapped in the cuticular wax and it is unlikely to be inhaled by consumers.

7. Cumulative Effects

Section 408(b)(2)(D)(v) of the FFDCA requires the Agency to consider the cumulative effects of exposure to *Candida oleophila* Strain O and to other substances that have a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. *Candida oleophila* Strain O is not toxic or pathogenic to mammals via several routes of exposure. Additionally, there are no other *Candida oleophila* strains currently registered as pesticides with the Agency. Consequently, since this microbial pesticide has no demonstrated toxicity, there is no reason to anticipate cumulative effects from the residues of this product with other related microbial pesticides.

8. Risk Characterization

The Agency considered human exposure to *Candida oleophila* Strain O in light of the standard for registration and safety factors in FIFRA and FFDCA, as amended by the FQPA. A determination has been made that no unreasonable adverse effects to the United States population in general, and to infants and children in particular, will result from the use of *Candida oleophila* Strain O when used in accordance with EPA-approved labeling.

C. Environmental Assessment

1. Ecological Hazards (40 CFR § 158.2150)

Adequate non-target toxicology data/information are available to support registration of NEXY, which contains *Candida oleophila* Strain O, for intended indoor uses on pome fruits (pears, apples). Because of these intended uses, direct exposures to most terrestrial and all aquatic environments are not expected, and therefore, all non-target toxicology data requirements for *Candida oleophila* Strain O were satisfied with appropriate data waiver requests and rationales.

Based on the summary data and information submitted in MRID No. 473138-15, *Candida oleophila* Strain O is not toxic to adult rainbow trout (*Oncorhynchus mykiss*) nor to freshwater cladocerans (*Daphnia magna*). As agreed by participants during a pre-registration conference held on November 21, 2006, only summary information of testing were submitted for the federal registration for intended indoor uses of *Candida oleophila* Strain O. If future uses include outdoor uses where exposures of non-target organisms would be increased, complete studies must be submitted and reviewed by appropriate

Agency personnel. Other data requirements may be triggered dependent on the intended uses and exposures to non-target organisms and the environment.

For a comprehensive guideline-by-guideline summary of the non-target toxicity data requirements, refer to Table 4 in Appendix A.

2. Environmental Fate and Ground Water Data

Tier II environmental fate and groundwater data requirements were not triggered because the product is labeled for indoor use on pome fruit (apples and pears) only. Furthermore, as agreed by participants during a pre-registration conference held on November 21, 2006, summary information of two studies were submitted for the federal registration: (1) soil survival "kinetics" and (2) survival in sterile distilled water by *Candida oleophila* Strain O.

(1) Survival of *Candida oleophila* Strain O in soil: The viability and survival of *Candida oleophila* Strain O was demonstrated in an *in vitro* study using two soil microcosms (acidic and limy-clay). After 115 days, it was reported that "this strain of yeast can survive in heat-treated soil at high density ($>10^5$ cfu/g soil)" and populations of this yeast did not increase when introduced into soils.

(2) Survival of *Candida oleophila* Strain O in sterile distilled water: The viability and survival of *Candida oleophila* Strain O decreased and disappeared after 21 days; in aqueous suspensions of 10^7 cells/milliliter (mL). It was reported that *Candida oleophila* Strain O is capable of surviving in freshwater lakes and sediments.

3. Ecological Exposure and Risk Characterization

No risks to non-target organisms or to the environment are anticipated as a result of the intended indoor uses of *Candida oleophila* Strain O.

4. Endangered Species Assessment

No risks to endangered species are anticipated as a result of the intended indoor uses of *Candida oleophila* Strain O.

V. ENVIRONMENTAL JUSTICE

The Environmental Protection Agency seeks to achieve environmental justice—the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income—with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. Fair treatment means that no group of people, including racial, ethnic, or socioeconomic groups, should bear a disproportionate share of the negative environmental consequences resulting from industrial, municipal,

and commercial operations or the execution of federal, state, local, and tribal environmental programs and policies. Meaningful involvement means that (1) potentially affected community residents have an appropriate opportunity to participate in decisions about a proposed activity that will affect their environment and/or health; (2) the public's contribution can influence the regulatory agency's decision; (3) the concerns of all participants involved will be considered in the decision-making process; and (4) the decision-makers seek out and facilitate the involvement of those potentially affected. EPA has this goal for all communities and persons across the United States.

At this time, the Environmental Protection Agency does not believe the use of NEXY, which contains *Candida oleophila* Strain O as an active ingredient, will cause harm or a disproportionate impact on at-risk communities.

For additional information regarding environmental justice issues, please visit EPA's web site at *http://www.epa.gov/compliance/environmentaljustice/index.html*.

VI. RISK MANAGEMENT AND REGISTRATION DECISIONS

A. Determination of Eligibility

Section 3(c)(5) of FIFRA permits for the registration of a pesticide provided that all the following determinations are made:

(1) Its composition is such as to warrant the proposed claims for it;
(2) Its labeling and other material required to be submitted comply with the requirements of FIFRA;
(3) It will perform its intended function without unreasonable adverse effects on the environment; AND
(4) When used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment.

To satisfy criterion 1, *Candida oleophila* Strain O has well-known properties. The Agency has no knowledge that would contradict the claims made on the NEXY label and *Candida oleophila* Strain O is not expected to cause unreasonable adverse effects when used according to the label instructions. Criterion 2 is satisfied by the current label and the data presented in this document. It is believed that *Candida oleophila* Strain O will not cause any unreasonable adverse effects, and it is likely to provide protection against blue and gray mold as claimed, satisfying criterion 3. Criterion 4 is satisfied in that *Candida oleophila* Strain O is not expected to cause unreasonable adverse effects when used according to label instructions. Therefore, NEXY, containing *Candida oleophila* Strain O as a new active ingredient, is eligible for registration under FIFRA section 3(c)(5) for the labeled uses. If the registrant proposes more extensive uses (e.g., outdoor uses), a registration amendment with additional data will be required.

B. Registration Review

The Federal Insecticide, Fungicide, and Rodenticide Act, as amended by the FQPA of 1996, mandated the continuous review of existing pesticides. All pesticides distributed and sold in the United States must generally be registered by the EPA, based on scientific data showing that they will not cause unreasonable risks to human health, workers, or the environment when used as directed in product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided at *http://www.epa.gov/oppsrrd1/registration_review/*.

The Agency has implemented the registration review program pursuant to FIFRA section 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. A registration review decision is the Agency's determination whether a pesticide meets, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act. *Candida oleophila* Strain O will be included in the schedule for registration review at the end of the Fiscal Year when schedules are updated.

C. Regulatory Decision

As of June 2009, the data requirements have been fulfilled for NEXY's labeled sites (Appendix B). Consequently, under FIFRA section 3(c)(5), the Biopesticides and Pollution Prevention Division recommends unconditional registration of the end-use product, NEXY, containing *Candida oleophila* Strain O as an active ingredient. Additionally, the toxicological database submitted in support of NEXY and *Candida oleophila* Strain O meets the safety requirements of the Food Quality Protection Act of 1996, provided that the end-use product is used as labeled; therefore, a permanent exemption from the requirement of a tolerance has been established for the residues of the microbial pesticide, *Candida oleophila* Strain O, on apples and pears when applied as a post-harvest biofungicide (40 CFR § 180.1289).

To mitigate the possibility for occupational exposure to *Candida oleophila* Strain O and potential for respiratory allergic sensitization, mixers and loaders working with NEXY must wear a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95, or P-95. Furthermore, although no adverse dermal effects have been reported by workers and dermal sensitization to operators is not anticipated, potential for dermal hypersensitivity incidents is mitigated by label requirements that a long-sleeved shirt, long pants, socks, shoes, and waterproof gloves be worn when mixing, loading, or applying the product or when handling crates containing treated apples and pears. Lastly, protective eyewear is also required when mixing, loading, or applying the product or when handling crates containing treated apples and pears because of exposure potential

and the results of the acute eye irritation study.

D. Labeling

The label for the registered end-use product containing the active ingredient, *Candida oleophila* Strain O, is available at http://oaspub.epa.gov/pestlabl/ppls.home**.**

VII. ACTIONS REQUIRED BY THE REGISTRANT

Before releasing pesticide products containing *Candida oleophila* Strain O for shipment, the registrant is required to provide appropriate final printed labeling to the Agency.

The Agency evaluated the data submitted in connection with the initial registration of an end-use product, NEXY, containing *Candida oleophila* Strain O as a new active ingredient. It was determined that these data fulfill current registration guideline requirements. No additional data are required to be submitted to the Agency at this time. For new uses and/or changes to existing uses, additional data may be required.

Notwithstanding the information stated in the previous paragraph, it should be clearly understood that certain, specific data are required to be reported to the Agency as a requirement for maintaining the federal registration for a pesticide product. A brief summary of these types of data are listed below.

A. Reporting of Adverse Effects

Reports of all incidents of adverse effects to the environment must be submitted to the Agency under the provisions stated in FIFRA section 6(a)(2).

B. Reporting of Hypersensitivity Incidents

Additionally, all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency under the provisions of 40 CFR § 158.2140(d).

VIII. GLOSSARY OF ACRONYMS AND ABBREVIATIONS

BCCM	Belgian Coordinated Collections of Microorganisms
BPPD	Biopesticides and Pollution Prevention Division
BRAD	Biopesticides Registration Action Document
CFR	Code of Federal Regulations
cfu	colony-forming unit
cm^2	square centimeter
°C	degrees Celsius
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EP	end-use product
EPA	Environmental Protection Agency (the "Agency")
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FR	Federal Register
g	gram
kg	kilogram
L	Liter
LC_{50}	median lethal concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air, or feed (e.g., mg/L, mg/kg, or ppm).
LLC	limited liability company
LOEC	lowest observable effect concentration
MRID No.	Master Record Identification Number
µm	micrometer
mg	milligram
mL	milliliter
mm	millimeter
MUCL	Mycothèque de l'Université Catholique de Louvain
NIOSH	National Institute for Occupational Safety and Health
NOEC	no observable effect concentration
OPP	Office of Pesticide Programs
OPPTS	Office of Prevention, Pesticides, and Toxic Substances
PII	Primary Irritation Index
P.O. Box	Post Office Box
PP	Pesticide Petition
PPE	personal protective equipment
TGAI	technical grade of the active ingredient

IX. BIBLIOGRAPHY

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APPENDIX A – MICROBIAL PESTICIDE DATA REQUIREMENTS

TABLE 1. Product Analysis Data Requirements for the Technical Grade of the Active Ingredient (TGAI), *Candida oleophila* Strain O, and Its Associated End-Use Product (EP), NEXY (40 CFR § 158.2120)

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
Product Chemistry and Composition			
Product Identity (885.1100)	Not applicable	*Candida oleophila* Strain O is a single-celled yeast in the phylum Ascomycota, the class Ascomycetes, and the family Saccharomycetaceae. Found naturally on plant tissues (fruits, flowers, and wood) and in water, it was originally isolated from golden delicious apples. NEXY, containing *Candida oleophila* Strain O, is intended for use as an antagonist to control the fungal pathogens, gray mold (*Botrytis cinerea*) and blue mold (*Penicillium expansum*), that cause post-harvest decay on apples and pears. The mode of action for *Candida oleophila* Strain O is primarily through competition for nutrients and pre-colonization of plant wound sites (Jijakli *et al.* 1993). Submitted data also suggest that production of beta-1,3-glucanases (i.e., hydrolytic enzymes that can degrade fungal phytopathogen cell walls) may contribute to its antagonistic activity. **Classification: Acceptable**	473138-05
Manufacturing Process (885.1200)	Submitted data satisfy the requirements of manufacturing process for both the TGAI and EP. **Classification: Acceptable**		473138-05
Deposition of a Sample in a Nationally Recognized Culture Collection (Not applicable)	*Candida oleophila* Strain O is on deposit with the Belgian Coordinated Collections of Microorganisms (BCCM)/Mycothèque de l'Université Catholique de Louvain (MUCL) in Louvain-la-Neuve, Belgium under Accession Number MUCL 40564.	Not applicable	473138-05
Discussion of Formation of Unintentional Ingredients (885.1300)	Submitted data satisfy the requirements of discussion of formation of unintentional ingredients for both the TGAI and EP. **Classification: Acceptable**		473138-05
Analysis and Certified Limits			
Analysis of Samples (885.1400)	Submitted data satisfy the requirements of analysis of samples for both the TGAI and EP. **Classification: Acceptable**		473138-05 473138-06

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
Certification of Limits (885.1500)	Not applicable	The certified limits for the active and inert ingredients exceed the OPPTS Guideline 830.1750 specified ranges, but an acceptable explanation was provided. **Classification: Acceptable**	Not applicable
Physical and Chemical Characteristics			
Color (830.6302)	Yellow	Not applicable	473138-01
Physical State (830.6303)	Solid (micro-granules)	Not applicable	473138-01
Odor (830.6304)	Yeast	Not applicable	473138-01
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions (830.6313)	Waived due to the dry basis of the product, the stability at normal temperatures, and packaging in non-metallic containers. **Classification: Acceptable**	Not applicable	473138-04
Storage Stability (830.6317)	6-month study at 20±2°C, the active ingredient was higher then the acceptance value (8.10×10^9 cfu/g), though a significant decrease was seen after 5 and 6 months of storage. 18-month study at 4±2°C, the active ingredient was higher then the acceptance value (6.10×10^9 cfu/g), though a significant decrease was seen at 18 months of storage.		473138-02 473138-03
Miscibility (830.6319)	Not applicable	Not required because NEXY is not an emulsifiable form of microbial pesticide (refer to test note #2 of 40 CFR § 158.2120(d)).	473138-04
Corrosion Characteristics (830.6320)	Not applicable	Waived because NEXY is a dry product on an inert carrier packaged in polyethylene materials highly resistant to corrosion. **Classification: Acceptable**	473138-04
pH (830.7000)	6.24 (1% weight/volume in water)	Not applicable	473138-01
Viscosity (830.7100)	Not applicable	Not required because NEXY is not a liquid form of microbial pesticide (refer to test note #4 of 40 CFR § 158.2120(d)).	473138-04
Density/Relative Density/Bulk Density (830.7300)	Bulk density = 0.597 kilogram (kg)/Liter (L) Tap density = 0.667 kg/L	Not applicable	473138-01

TABLE 2. Toxicology Data Requirements for the Technical Grade of the Active Ingredient (TGAI), *Candida oleophila* Strain O, and Its Associated End-Use Product (EP), NEXY (40 CFR § 158.2140)

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
Tier I			
Acute Oral Toxicity/Pathogenicity (885.3050)	Not toxic, infective, and/or pathogenic to rats by oral dose of 2.3–3.8 x 10^8 cfu/animal. **Classification: Acceptable**	Not applicable	473138-07
Acute Pulmonary Toxicity/Pathogenicity (885.3150)	Not toxic, infective, and/or pathogenic to rats by pulmonary dose of 1.2–5.2 x 10^8 cfu/animal. **Classification: Acceptable**	Not applicable	473138-09
Acute Injection Toxicity/Pathogenicity (885.3200)	Not toxic, infective, and/or pathogenic to rats by subcutaneous dose of 1.1–2.0 x 10^7 cfu/animal. **Classification: Acceptable**	Not applicable	473138-08
Hypersensitivity Incidents (885.3400)	During a pilot-plant production trial of NEXY using fermentation vessels and involving large amounts of *Candida oleophila* Strain O, three of six workers not wearing personal protective equipment reported clinical symptoms of a respiratory reaction. No adverse dermal effects have been reported by workers. Potential for hypersensitivity incidents has been mitigated by label requirements that a long-sleeved shirt, long pants, socks, shoes, and waterproof gloves be worn when mixing, loading, or applying the product or when handling crates containing treated apples and pears. Additionally, mixers and loaders must wear a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95, or P-95. Any future hypersensitivity incidents must be reported per OPPTS Guideline 885.3400.		473138-12
Cell Culture (885.3500)	Not required because *Candida oleophila* Strain O is not a virus (refer to test note #4 of 40 CFR § 158.2140(d)).	Not applicable	Not applicable
Acute Oral Toxicity (870.1100)	Not applicable	Waived based on the results of MRID Number 473138-07 and the nature of the inert ingredients in NEXY's formulation. **Classification: Acceptable TOXICITY CATEGORY IV**	475610-01
Acute Dermal Toxicity (870.1200)	Not applicable	Waived based on the results of MRID Numbers 473138-08 and 473138-11 and the nature of the inert ingredients in NEXY's formulation. **Classification: Acceptable TOXICITY CATEGORY III**	473227-01

Data Requirement (OPPTS Guideline)	Results		MRID Number
	TGAI	EP	
Acute Inhalation Toxicity (870.1300)	Not applicable	Waived based on the results of MRID Number 473138-09 and the nature of the inert ingredients in NEXY's formulation. **Classification: Acceptable TOXICITY CATEGORY III**	475610-01
Acute Eye Irritation (870.2400)	Not applicable	NEXY was minimally irritating to rabbits at a dose of 100 mg/animal. **Classification: Acceptable TOXICITY CATEGORY III**	473138-10
Primary Dermal Irritation (870.2500)	Not applicable	NEXY was not irritating to rabbits at a dose of 0.5 g/animal. **Classification: Acceptable TOXICITY CATEGORY IV**	473138-11
Tiers II and III			
Not required for *Candida oleophila* Strain O based on the lack of acute toxicity/pathogenicity in the Tier I studies.			

TABLE 3. Additional Studies Submitted to Support the Registration of the End-Use Product (EP), NEXY, Containing *Candida oleophila* Strain O as an Active Ingredient

Data Requirement (OPPTS Guideline)	Results	MRID Number
Mutagenicity Testing		
Bacterial Reverse Mutation Assay (870.5100)	Indicates *Candida oleophila* Strain O does not have mutagenic potential. **Classification: Supplemental (Not a required study for this active ingredient)**	473138-13
In vitro Mammalian Cell Assay (870.5300)	Indicates *Candida oleophila* Strain O does not have mutagenic potential. **Classification: Supplemental (Not a required study for this active ingredient)**	473138-14

TABLE 4. Non-Target Organisms and Environmental Fate Data Requirements for the Technical Grade of the Active Ingredient (TGAI), *Candida oleophila* Strain O (40 CFR § 158.2150)

Data Requirement (OPPTS Guideline)	Results	Toxicity Category/Description	MRID Number
Tier I			
Avian Oral Toxicity (885.4050)	Not required for the intended indoor use pattern (refer to test note #1 of 40 CFR § 158.2150(e)). Submitted waiver rationale was **Acceptable**.	Not applicable	473138-15
Avian Inhalation Toxicity/Pathogenicity (885.4100)	Not required for the intended indoor use pattern (refer to test note #1 of 40 CFR § 158.2150(e)). Submitted waiver rationale was **Acceptable**.	Not applicable	473138-15
Wild Mammal Toxicity/Pathogenicity (885.4150)	Not required for the intended indoor use pattern. Submitted waiver rationale was **Acceptable**.	Not applicable	473138-15
Freshwater Fish Toxicity/Pathogenicity (885.4200)	Not required for the intended indoor use pattern (refer to test note #1 of 40 CFR § 158.2150(e)). Submitted waiver rationale was **Acceptable**. Submitted summary information indicated no mortalities on adult rainbow trout under semi-static, daily water renewal conditions. The reported median lethal concentration (LC_{50}) was greater than 333 mg TGAI/L after 96 hours.	Not acutely toxic to adult rainbow trout[1]	473138-15
Freshwater Invertebrate Toxicity/Pathogenicity (885.4240)	Not required for the intended indoor use pattern (refer to test note #1 of 40 CFR § 158.2150(e)). Submitted waiver rationale was **Acceptable**. Submitted summary information indicated no mortalities on adult daphnids under semi-static, frequent renewal conditions. The reported no observable effect concentration (NOEC) (measured) was equal to 15.7 mg TGAI/L; reported lowest observable effect concentration (LOEC) (measured) was greater than 15.7 mg TGAI/L after 21 days.	Not toxic to adult daphnids[1]	473138-15

[1] Only summary information of testing were submitted for the federal registration for intended indoor uses of *Candida oleophila* Strain O, as agreed by participants during a pre-registration conference held on November 21, 2006.

Data Requirement (OPPTS Guideline)	Results	Toxicity Category/Description	MRID Number
Estuarine/Marine Fish Testing Estuarine and Marine Invertebrate Testing (885.4280)	Not required for the intended indoor use pattern.	Not applicable	Not applicable
Non-Target Plant Testing (885.4300)	Not required for the intended indoor use pattern (refer to test note #1 of 40 CFR § 158.2150(e)). Submitted waiver rationale was **Acceptable**.	Not applicable	473138-15
Non-Target Insect Testing (885.4340)	Not required for the intended indoor use pattern. Submitted waiver rationale was **Acceptable**.	Not applicable	473138-15
Honey Bee Testing (885.4380)	Not required for the intended indoor use pattern. Submitted waiver rationale was **Acceptable**.	Not applicable	473138-15
Tiers II, III, and IV			
Not required for *Candida oleophila* Strain O because its associated end-use product, NEXY, is labeled for indoor use on pome fruit (apples and pears) only.			

APPENDIX B – *CANDIDA OLEOPHILA* STRAIN O END-USE PRODUCTS

EPA Registration Number	Registration Name	Percentage Active Ingredient	Formulation Type	Use Site	Method of Application	Application Rate	Target Pests
84863-1	NEXY	57.0%	Dilutable Powder	Indoor (Apples and Pears)	Dip or Drench	0.9 ounces of NEXY and 5.4 ounces of NEXY ADDITIVE per 20 gallons of water 2.4 to 7.3 gallons of mixture per ton of apples or pears	Gray Mold (*Botrytis cinerea*) and Blue Mold (*Penicillium expansum*)