Candida oleophila
PC Codes 021008 and 021010

Interim Registration Review Decision
Case Number 6019

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I. Introduction

This document is the Environmental Protection Agency's (EPA or the Agency) Interim Registration Review Decision for *Candida oleophila* (Case 6019, PC codes 021008 and 021010), and is being issued pursuant to 40 CFR §§ 155.50 and 155.58. This case includes the active ingredients *Candida oleophila* strain O and *Candida oleophila* isolate I-182, hereafter referred to as *Candida oleophila*. These active ingredients were grouped into one registration review case pursuant to 40 CFR § 155.42(a). 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 (FIFRA). The Agency may issue, when it determines it to be appropriate, an interim registration review decision before completing a registration review. Among other things, the interim registration review decision may: 1) require new risk mitigation measures; 2) impose interim risk mitigation measures; 3) identify data or information required to complete the review; and 4) establish schedules for submitting the required data, conducting the new risk assessment, and completing the registration review.

FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States generally must be registered by the Agency based on scientific data showing that they will not cause unreasonable adverse effects to human health or to the environment when used as directed on product labeling. The registration review program is intended to ensure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically re-evaluates pesticides to ensure that as these changes occur, products in the marketplace can continue to be used safely. Information on this program is provided at www.epa.gov/pesticide-reevaluation. In 2006, the Agency implemented the registration review program pursuant to FIFRA § 3(g). The Agency will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

The regulations governing registration review are provided in 40 CFR part 155, subpart C. The public phase of registration review begins when the initial docket is opened for the case. The docket is the Agency's opportunity to inform the public what it knows about *Candida oleophila* and what additional risk analyses and data or information, if any, it believes are needed to make a registration review decision on *Candida oleophila*. Additional information on *Candida oleophila* can be found in the Agency's public docket (EPA-HQ-OPP-2022-0445) at www.regulations.gov.

This document is organized into five sections: the *Introduction*, which includes this summary and the *Candida oleophila* case overview; *Use Information*, which describes how and why *Candida oleophila* is used and summarizes data on its use, and associated pesticide product; *Scientific Assessments*, which summarizes the Agency's risk assessments, any revisions, and risk conclusions; *Interim Registration Review Decision*, which describes the regulatory rationale for the Agency's interim registration review decision; and, lastly, the *Next Steps* and *Timeline* provides an anticipated timeline for completion of this registration review case.

Candida oleophila Registration Review Case Overview

Pursuant to 40 CFR § 155.50, the Agency formally initiated registration review for *Candida oleophila* (Case 6019). The following list highlights significant events that have occurred during the current cycle of registration review for this case. Documentation of these events can be found in the Agency's public docket for this registration review case in docket EPA-HQ-OPP-2022-0445 available at www.regulations.gov.

- July 13, 2022 – Publication of the *Candida oleophila Combined Preliminary Work Plan and Proposed Interim Registration Review Decision* (PWP PID) for a 60-day public comment period. The comment period closed September 13, 2022. The Agency received one public comment, from the United States Department of Agriculture. This comment was in support of the Agency's PWP PID for *Candida oleophila*.
- December 2022 – The Agency is now publishing the *Candida oleophila Interim Registration Review Decision.*

II. Use Information

The first pesticide product containing *Candida oleophila* strain O as an active ingredient was registered by the Agency in 2009. Currently, there is one registered end-use product containing *Candida oleophila* strain O at 57% active ingredient. The last product containing *Candida oleophila* isolate I-182 (PC code 021008) was cancelled in 2004. Therefore, *Candida oleophila* isolate I-182 was neither assessed nor is it discussed further in this document.

Candida oleophila is a single-celled yeast found naturally on plant tissues of fruits, flowers, wood, and in water. As a pesticide, it 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* is primarily through competition for nutrients and pre-colonization of plant wound sites, and 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 (U.S. EPA, 2009).

Table 1. *Candida oleophila* Use Information

Ingredient Name	*Candida oleophila*
PC Code	021010
Pesticide Classification	Fungicide
Use Site Locations	Occupational/manufacturing/processing/industrial area (indoor)
Application Types	Spray drench; dip treatment
No. of Registrations	1 FIFRA Section 3 product[1]
Physical Forms	Dust/powder

III. Scientific Assessments

A summary of the Agency's human health and ecological risk assessments for *Candida oleophila* is presented below. Refer to the Appendices for a listing of product analysis, human health assessment, and nontarget organism data that support the scientific assessments for this registration review. For further information on the human health and environmental risk assessments, including a summary of data and literature search findings, please see Appendices B and C.

A. Human Health Assessment

Hazard Characterization

The human health toxicological database is considered complete for characterizing hazard and assessing risk from the active ingredient in this case. In acute oral and pulmonary toxicity/pathogenicity testing, *Candida oleophila* demonstrated no toxicity, pathogenicity, or infectivity. *Candida oleophila* is not expected to cause significant eye or skin irritation based on testing of the end-use product (U.S. EPA, 2009). The Agency does not anticipate the need for additional studies for this registration review action,

[1] FIFRA labels can be obtained from the Pesticide Product Label System (ordspub.epa.gov/ords/pesticides/f?p=PPLS:1)

as all data requirements per 40 CFR § 158.2140 have been fulfilled for *Candida oleophila*. All supporting data, Agency risk assessments, and other information on this active ingredient were evaluated against standards established by FIFRA and the Agency's regulations and scientific policies.

Dietary Exposure and Risk Characterization

Dietary exposure to *Candida oleophila* is likely to occur, mainly through food. However, *Candida oleophila* is common on numerous types of foods that are regularly consumed without adverse effects. The practices of washing, peeling, and processing fruits further reduce the potential for residues of *Candida oleophila* and minimize dietary exposure. Exposure through drinking water is not expected, as the product is not applied directly to bodies of water, and if it were to reach ground water, it would likely be removed or inactivated during the drinking water treatment process. Furthermore, if exposure were to occur through food or drinking water sources, *Candida oleophila* is not known to grow at human body temperatures, and the acute oral and pulmonary toxicity/pathogenicity studies showed no toxic or pathogenic effects in rats (U.S. EPA, 2009).

Food Tolerances

Considering the available toxicity and exposure data discussed above, EPA concluded that there was a reasonable certainty that no harm would result to the U.S. population from aggregate exposure to residues of *Candida oleophila* when used according to label directions. Therefore, EPA established a tolerance exemption for residues of the active ingredient. The current tolerance exemption is stated as follows:

> **40 CFR § 180.1289 *Candida oleophila* Strain O; exemption from the requirement of a tolerance.** An exemption from the requirement of a tolerance is established for the residues of the microbial pesticide, *Candida oleophila* Strain O, on apples and pears when applied/used as a post-harvest biofungicide. [74 FR 22464, May 13, 2009]

Residential and Non-Occupational Exposure and Risk Characterization

Candida oleophila is intended only for indoor, post-harvest agricultural use. Therefore, exposure to *Candida oleophila* from pesticidal use is not expected in non-occupational or residential settings.

Occupational Exposure and Risk Characterization

Occupational exposures to *Candida oleophila* are likely during the indoor, post-harvest applications. However, these dip, drench, and spray applications are not expected to result in exposures of concern considering the results of the toxicity data supporting the registration of this active ingredient and the use of required personal protective equipment (PPE). The required PPE includes a long-sleeved shirt, long pants, socks, shoes, protective eyewear, waterproof gloves, and a NIOSH-approved respirator.

Regarding occupational incidents, a report was submitted to the Agency indicating that three workers exhibited clinical symptoms of a respiratory reaction (U.S. EPA, 2009). This incident involved three workers exposed to a large amount of *Candida oleophila* during a pilot-plant production trial involving work on fermentation vessels without the use of PPE. However, the type and degree of exposures involved in this incident are not considered relevant to worker exposures resulting from use of this pesticide, and no other incidents resulting from this active ingredient have been reported. Worker and handler exposure to *Candida oleophila* is not expected to pose any undue risk when used in accordance with the precautions and restrictions on the product labeling.

Human Incidents

Other than the occupational incidents described above, no incidents associated with *Candida oleophila* have been reported to the Agency. A search of the Office of Pesticide Programs' (OPP) Incident Data System conducted on May 9, 2022, revealed no reported incidents associated with *Candida oleophila*. This database contains information dating back to the 1970s and is continuously updated as incidents are reported.

B. Environmental Risk Assessment

All nontarget organism and environmental fate data necessary to meet the standard for *Candida oleophila* were satisfied through the acceptance of waiver rationales that described the exclusive indoor use of the active ingredient. Indoor uses will not result in any exposure to nontarget organisms. Based on lack of exposure, risk to nontarget organisms is not expected. Furthermore, testing data was provided for freshwater fish and invertebrates, showing a lack of toxicity and adverse effects. Due to the exclusively indoor uses, risk to pollinators is also not expected as a result of the pesticidal use of *Candida oleophila.*

Ecological Incidents

A search of OPP's Incident Data System conducted on May 9, 2022, revealed no reported incidents associated with *Candida oleophila*. This database contains information dating back to the 1970s and is continuously updated as incidents are reported.

Endangered Species Assessment

EPA has no reasonable expectation for any registered use of *Candida oleophila* to cause direct or indirect discernible effects to threatened and endangered species or their designated critical habitat. This is because, based on the lack of exposure from the indoor use pattern, exposure to listed species or their designated critical habitat is not expected. Therefore, EPA has made a "No Effect" determination under the Endangered Species Act (ESA) for all listed species and designated critical habitats for such species and has therefore concluded that consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service under ESA section 7(a)(2) is not required.

IV. Interim Registration Review Decision

In accordance with 40 CFR §§ 155.56 and 155.58, the Agency is issuing this *Interim Registration Review Decision*. Except for the Endocrine Disruptor Screening Program (EDSP) component of this case, the Agency has made the following interim decisions: (1) no additional data are required at this time; and (2) no changes to the affected registrations and their labels are needed at this time.

In this interim decision, the Agency is making no human health or environmental safety findings associated with the EDSP screening of *Candida oleophila*. The Agency's final registration review decision for *Candida oleophila* will be made following satisfaction of the EDSP obligations under FFDCA § 408(p).

V. Next Steps and Timeline

A Federal Register Notice will announce the availability of this *Interim Registration Review Decision*. The Agency's final decision on the *Candida oleophila* registration review case will occur following satisfaction of the EDSP obligations under FFDCA § 408(p).

Table 2. Anticipated Registration Review Schedule for *Candida oleophila*	
Anticipated Activity	**Estimated Month/ Year**
Open Docket and 60-Day Public Comment Period for Combined Preliminary Work Plan and Proposed Interim Registration Review Decision	July 2022
Close Public Comment Period	September 2022
Issue Interim Registration Review Decision	December 2022
Final Decision*	TBD

*The anticipated schedule will be revised as necessary (e.g., need arising under the Endocrine Disruptor Screening Program with respect to the active ingredients in this case).

Appendix A – Summary of Existing Product Analysis Data

The available product chemistry data for *Candida oleophila* are considered acceptable. Table 3 summarizes the current product analysis data requirements and results supporting registration review of *Candida oleophila*.

Table 3. Summary of Product Analysis Data (40 CFR § 158.2120)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Product Identity	885.1100	Acceptable	47313805
Manufacturing Process	885.1200	Acceptable	47313805
Deposition of a Sample in a Nationally Recognized Culture Collection	885.1250	Acceptable	47313805
Discussion of Formation of Unintentional Ingredients	885.1300	Acceptable	47313805
Analysis of Samples	885.1400	Acceptable	47313805
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions	830.6313	Acceptable	47313804
Storage Stability	830.6317	Acceptable	47313802 47313803 47313804
pH	830.7000	Acceptable	47313801
Density/Relative Density/Bulk Density (Specific Gravity)	830.7300	Acceptable	47313801

Appendix B – Summary of Mammalian Toxicology Data

The human health toxicological database is considered complete for characterizing hazard and assessing risk from the active ingredient in this case. Tables 4 summarizes the current mammalian toxicology data requirements and results supporting registration review of *Candida oleophila*.

Table 4. Summary of Toxicology Data (40 CFR § 158.2140)

Data Requirement	OCSPP Guideline No.	Results / Findings	MRIDs
Acute Oral Toxicity/Pathogenicity	885.3050	Acceptable Not toxic, infective, and/or pathogenic to rats by oral dose of 2.3 – 3.8 x 10^8 CFU/animal.	47313807
Acute Pulmonary Toxicity/Pathogenicity	885.3150	Acceptable Not toxic, infective, and/or pathogenic to rats by pulmonary dose of 1.2 – 5.2 x 10^8 CFU/animal	47313809
Acute Injection Toxicity/Pathogenicity	885.3200	Acceptable Not toxic, infective, and/or pathogenic to rats by subcutaneous dose of 1.1 – 2.0 x 10^7 CFU/animal.	47313808
Hypersensitivity Incidents	885.4300	Acceptable	47313812
Cell Culture	885.3500	N/A	N/A

Literature Search Findings

To support registration review, the Biopesticides and Pollution Prevention Division (BPPD) conducts searches of the literature and incident databases to determine if there are any reports of adverse effects that might change risk conclusions or change knowledge of the state of the science for *Candida oleophila*. Searches conducted for *Candida oleophila* are described below.

Human Health Results:

A literature search was conducted with the PubMed and Web of Science search engines using the term "*Candida oleophila*" crossed with the terms "pathogen," "disease," "infection," and "zoonoses." The first three search terms produced results ranging from 10 to 116 articles, while the "zoonoses" search did not produce any results. A large majority of these search results were associated with agricultural research and post-harvest uses of Candida oleophila. None of the search results indicated the potential for adverse human health effects. As a result, no additional information was gained from these searches that would alter the BPPD's understanding of the current state of the science for any potential effects of *Candida oleophila* on humans.

Appendix C – Summary of Nontarget Organism Data

All nontarget organism and environmental fate data necessary to meet the standard for *Candida oleophila* were satisfied through the acceptance of waiver rationales that described the exclusively indoor uses of the active ingredient. Based on the current ecological exposure information for the uses of *Candida oleophila*, the Agency has determined that a new ecological risk assessment is not needed for this case. Table 6 summarizes the current nontarget organism data requirements and results supporting registration review of *Candida oleophila*.

Table 6. Summary of Nontarget Organism Data (40 CFR § 158.2150)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Avian oral toxicity	885.4050	Requirement waived based on indoor use pattern	47313815
Avian inhalation toxicity/pathogenicity	885.4100		
Wild mammal toxicity/pathogenicity	885.4150		
Freshwater fish toxicity/ pathogenicity	885.4200		
Freshwater invertebrate toxicity/pathogenicity	885.4240		
Estuarine/Marine fish testing Estuarine/Marine invertebrate testing	885.4280		
Nontarget plant testing	885.4300		
Nontarget plant testing	885.4300		
Nontarget insect testing	885.4340		

Literature Search Findings

To support registration review, BPPD conducts searches of the literature and incident databases to determine if there are any reports of adverse effects that might change risk conclusions or change knowledge of the state of the science for *Candida oleophila*. Searches conducted for *Candida oleophila* are described below.

Ecological Results:

A literature search for ecological adverse effects was not performed since the indoor use pattern is not expected to result in environmental exposure.

Appendix D – Endocrine Disruptor Screening Program (EDSP)

As required by FIFRA and the Federal Food, Drug, and Cosmetic Act (FFDCA), EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, sub-chronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental, and reproductive effects in different taxonomic groups. As part of its most recent registration decision for the *Candida oleophila* case, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA § 408(p), chemicals in the *Candida oleophila* case are subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where the Agency will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA § 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, the Agency issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The Agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013,[2] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. The active ingredient in this case is not on either list. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit the Agency website.[3]

In this interim decision, EPA is making no human health or environmental safety findings associated with the EDSP screening of *Candida oleophila*. Before completing this registration review, the Agency will make an EDSP FFDCA section 408(p) determination.

[2] See www.regulations.gov/document/EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[3] www.epa.gov/endocrine-disruption

References

U.S. EPA. (2009, July 15). *Biopesticides Registration Action Document. Candida oleophila Strain O*. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P10063FM.txt

U.S. EPA. (2020, December 31). *Environmental Risk Assessment for a FIFRA Section 3 Registration of a New Use for the Currently Registered End Use Product, Nexy, which Contains the Currently Registered Active Ingredient Candida oleophila Strain O.* Memorandum from Sarah Butler to Jennifer Odom.