BIOPESTICIDE REGISTRATION ACTION DOCUMENT

Laminarin

PC Code: 123200

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

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BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

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I. EXECUTIVE SUMMARY

Laminarin is a common component of the human diet. It is a naturally occurring polysaccharide carbohydrate (oliggosaccharide) found in all edible plants. It is a major constituent in cereal grains, and is consumed as an intentionally added ingredient in many dietary supplements and texturing agents. Laminarin is typically extracted from brown algae, where it is present in great quantity as a storage glucan – a carbohydrate food reserve that can be converted to glucose when necessary. The extraction results in a low-odor white powder, which is extremely nutrient rich. Besides being the source for this biochemical pesticide, this algal extract is also a regular ingredient in the Japanese diet. As a biochemical pesticide active ingredient, Laminarin stimulates the natural defense reactions of agricultural crops such as fruiting vegetables, tomato, eggplant, pepper, zucchini, cucurbits, watermelon, melons, grape, apple, pear, and strawberries against such disease organisms as gray mold, powdery mildew, downy mildew, fire blight, and bacterial spot. As a naturally occurring oligosaccharide, residues of the active ingredient are indistinguishable from other naturally occurring plant oligosaccharides. In addition to the long history of human consumption of Laminarin without known toxicological effect, data and information submitted to the Agency in conjunction with the petition for the exemption from a requirement of tolerance confirm that Laminarin is virtually non-toxic and poses no dietary risks to humans.

Acute, subchronic and developmental studies submitted in the application for registration provided sufficient information to satisfy all mammalian toxicology data requirements. No toxicological endpoints were established, and no adverse effects were observed with regard to mammalian health.

Because Laminarin is considered to be “toxicologically innocuous,” no residue studies are required to support an exemption from the requirement of a tolerance. Laminarin’s low toxicity profile notwithstanding, another justification for an exemption from the requirement of a tolerance is the minimal likelihood of residues for this biochemical pesticide. Laminarin is intended for application as a Systemic Acquired Resistance (SAR) inducer – a preventative mode of action. As such, it is applied early in a crop’s life cycle – in its growing stages - to help build immunity to disease organisms such as mold and bacterial infection. And as a biochemical, it biodegrades rapidly. Data indicate that the active ingredient is more than 65% biodegraded after two weeks (MRID 47264954). Calculations indicate that it would be largely biodegraded long before any final application would be practicable. Accordingly, no significant exposures are expected at the time of harvest.

No dietary risks are expected with regard to the use of the active ingredient Laminarin. Significant dietary exposures (including exposures via drinking water) are not expected for the active ingredient Laminarin. In the event of dietary exposure, the toxicological data demonstrate that Laminarin is not toxic or pathogenic to mammals. It is a regular constituent of the human diet; and there have been no health effects associated with its consumption by people. Furthermore, all data demonstrate that no acute, sub-chronic, chronic, immune, or endocrine-

disrupting effects are associated with the use of the active ingredient. Accordingly, no harm to infants, children, and the general U.S. population is anticipated with regard to dietary exposure. Because of the nontoxic profile and the lack of expected residue of the active ingredient, the risks associated with the proposed food uses of this active ingredient are expected to be negligible.

The potential for aggregate, non-occupational exposure is expected to be insignificant as the active ingredient is largely biodegraded within two weeks, and applications of Laminarin occur early in the growing season. Moreover, given a lack of acute toxicological endpoints and because Laminarin is not known to share any structural similarity to any chemicals with common mechanisms of toxicity, the likelihood of risks resulting from such de minimis exposures is negligible.

Non-target organism and environmental fate data requirements were satisfied by valid studies. Laminarin occurs naturally in the terrestrial environment, and is not associated with any known detrimental effect. All information available to the Agency validates a non-toxic mode of action, and a lack of adverse effect relative to non-target organisms.

In accordance with T-REX Model, the Individual Effects Chance Model Version 1.1 and the non-target data submitted, the Agency has made a "No Effect" (NE) determination for direct and indirect effects to any listed threatened and endangered species and their habitat as a result of the proposed uses of Laminarin.

On October 1, 2009, EPA announced a new policy to provide a more meaningful opportunity for the public to participate on major registration decisions before they occur. According to this new policy, EPA will provide a public comment period prior to making a registration decision for, at minimum, the following types of applications: new active ingredients, first food use, first outdoor use, first residential use, and other actions for which we anticipate significant public interest. The registration application for Laminarin is for a "new active ingredient" whose registration would result in a "first outdoor use" and a "first food use." Therefore, consistent with the new policy of making registration actions more transparent, the Agency provided a 30-day comment period on the Laminarin application and EPA's preliminary risk assessment. EPA did not receive any comments during the comment period.

EPA believes, based on the risk assessment and information submitted in support of the registration of Laminarin, that it is in the best interests of the public and the environment to issue the registration for Laminarin. The basis for this preliminary decision can be found in the risk assessment for Laminarin, which is characterized in this BRAD. As discussed above, acute toxicity data for Laminarin indicate a nontoxic profile. Laminarin does not demonstrate subchronic or developmental toxicity, and it is not mutagenic or genotoxic. EPA has no concerns for any non-target organisms exposed to Laminarin in accordance with approved label directions. EPA has not identified any toxic endpoints for non-target mammals, birds, plants, aquatic, or soil organisms. Nor are there concerns for any threatened and endangered species.

Thus, given that Laminarin has very low toxicity, and presents little if any risk to non-target organisms, and data confirm its effectiveness as a Systemic Acquired Response (SAR) Inducer, EPA concludes that it is in the best interests of the public and the environment to issue the registration for Laminarin.

EPA reviewed data requirements for granting registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). It was determined that the data/information submitted fulfilled current data requirements (refer to 40 CFR Subpart U § 158.2000).

II. ACTIVE INGREDIENT OVERVIEW

Common Name: Laminarin

Chemical Names: Oligosaccharide, Polysaccharide Carbohydrate, Glucan

Trade & Other Names: Laminarin

CAS Registry Number: 9008-22-4

OPP Chemical Code: 123200

Type of Pesticide: SAR Inducer

III. REGULATORY BACKGROUND

On July 31, 2008, EPA published in the Federal Register (Volume 74, Number 49) a notice announcing that Laboratoires Goemar SA, Z.AC La Madeline, Avenue General Patton, 35400 Saint-Malo, France c/o SciReg, Inc. 12733 Director's Loop, Woodbridge, VA 22192, submitted an application proposing to establish an exemption from the requirement of a tolerance for residues of the biochemical pesticide, Laminarin, in or on all food commodities (PP# 7E7276). On March 16, 2009, EPA published in the Federal Register (Volume 74, Number 49) a notice announcing that Laboratoires Goemar SA, Z.AC La Madeline, Avenue General Patton, 35400 Saint-Malo, France c/o SciReg, Inc. 12733 Director's Loop, Woodbridge, VA 22192, submitted an application to register a pesticide product (EPA File Symbol 83941-E) containing a new active ingredient (Laminarin) not included in any currently registered products. No comments were received following the publication of either notice. In addition, on January 5, 2010, EPA provided the opportunity for a 30-day comment period on the Agency's draft risk assessment and intention to register this pesticide product. EPA has not received any comment on this proposed action.

A. CLASSIFICATION

Laminarin is a naturally occurring polysaccharide carbohydrate present in most plants. With regard to its active properties, it is considered to be a SAR inducer, bolstering plant defense mechanisms, protecting plants against attacks from mold, bacteria and fungi. It does not work directly against pests, and is not associated with any toxic mode of action. Accordingly, Laminarin is considered to be a biochemical pesticide due to its nontoxic mode of action to the target pest, its natural occurrence in the environment, and its history of exposure to humans and the environment without known toxicity.

B. FOOD CLEARANCES/TOLERANCES

This active ingredient is being supported for food use. The Agency's risk assessment finds no evidence of dietary risk and supports Pesticide Petition# 7E7276, which proposes to establish an exemption from the requirement of a tolerance for residues of the biochemical pesticide, Laminarin, in or on all food commodities

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 Biopesticide Registration Action Document (BRAD) were considered in light of these requirements.

Classifications 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 the acute toxicity data requirements, toxicity categories are assigned for providing the appropriate precautionary labeling statement, based on the hazard(s) identified from studies and/or other information submitted to the Agency in support of a pesticide registration. The active ingredient or particular 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 ASESSMENT

1. Product Chemistry and Composition

Laminarin is a naturally occurring oligosaccharide that can be found in most plants. It serves plants as a storage glucan - a carbohydrate food reserve - which breaks down into glucose and provides energy when plants are stressed. Laminarin extract is derived from brown algae (Laminara *digitata*), and is a low-odor white powder. Because of its nutrient richness and starchy character, Laminarin extract is commonly used as a dietary supplement, a food texturing agent and an ingredient in some ethnic cuisines.

All product chemistry data requirements for Laminarin have been satisfied. As an active ingredient, Laminarin extract is indistinguishable from the oligosaccharide that is produced naturally in pants. The extract has a high degree of purity and contains no impurities of toxicological significance. All data requirements for physical and chemical characteristics have been adequately addressed.

2. Analysis and Certification of Limits

The submitted data satisfied the requirement for Analysis and Certification of Limits. Five batch analyses and the analytical method used to determine the purity of Laminarin were examined and determined to be acceptable by the Agency. The certified limits for the active and inert ingredients fall within the ranges specified by OPPTS Guideline 830-1750**.**

3. Physical and Chemical Characteristics

The Agency has determined that the submitted data adequately describe the physical and chemical characteristics of Laminarin. Refer to Table 1 in Appendix A for The Series 830 physical and chemical properties.

B. HUMAN HEALTH ASSESSMENT

1. Toxicological Hazard Assessment

Adequate mammalian toxicology studies were provided in support of the registration of Laminarin for each data requirement. Acute toxicology data for Laminarin indicates that the active ingredient is virtually non-toxic to mammals, and that there are no toxicological endpoints relative to the use of Lamanarin as a SAR inducer. Accordingly, the data submitted demonstrate that the proposed uses of Laminarin pose no significant risks to human health and support a

finding of reasonable certainty that no harm to the general U.S. population, including infants and children, will result from exposure to this active ingredient.

Refer to Table 2 in Appendix A for a summary of the Toxicity Data Requirements for this food use active ingredient.

a. Acute Toxicity – Tier I (40 CFR § 158.2050)

Acute Oral Toxicity – Rat [OPPTS Guideline 870.1100; Master Record Identification (MRID) Numbers (Nos.) 47264930 and 47264943]: An acute oral toxicity study shows that the active ingredient Laminarin has an LD_{50} of greater than 2000 mg/Kg in rats. This was the maximum dose rate. There were no observed toxicological effects on the test subjects at the maximum dose. The study supports the finding that this active ingredient poses no significant human health risk with regard to food uses. The study was found "ACCEPTABLE" and Laminarin was classified as TOXICITY CATEGORY III for this route of exposure when used as a SAR inducer.

Acute Dermal Toxicity– Rabbits (OPPTS Guideline 870.1200; MRID Nos. 47264931 and 47264974): An acute oral toxicity study shows that the active ingredient Laminarin has an LD_{50} of greater than 5000 mg/Kg in rats, which is considered to be virtually non-toxic. Data substantiate the active ingredient's relative dermal non-toxicity to both occupational users and the general public. The study was found "ACCEPTABLE" and Laminarin was classified as TOXICITY CATEGORY IV for this route of exposure when used as a SAR inducer.

Acute Inhalation Toxicity (OPPTS Guideline 870.1300; MRID Number (No.). 47264932): An acute oral inhalation study shows that the active ingredient Laminarin has an LC_{50} of greater than 1.02 mg/L in rats, which shows no significant inhalation toxicity. This was the maximum dose rate, and no toxicological effects were observed on the test subjects. The study was found "ACCEPTABLE" and Laminarin was classified as TOXICITY CATEGORY III for this route of exposure when used as a SAR inducer.

Primary Eye Irritation (OPPTS Guideline 870.2400; MRID Nos. 47264933 and 47264976): A primary eye irritation study on rabbits demonstrated Laminarin to be non-irritating. There were no observed effects for this route of exposure relative to the use of Laminarin. The study was found "ACCEPTABLE" and Laminarin was classified as TOXICITY CATEGORY IV for this route of exposure when used as a SAR inducer.

Primary Dermal Irritation (OPPTS Guideline 870.2500; MRID No. 47264934): A skin irritation study on rabbits demonstrated that Laminarin was not irritating to the skin. The findings are consistent with the other dermal studies and confirm that Laminarin is not toxic through this route of exposure. The study was found "ACCEPTABLE" and Laminarin was classified as TOXICITY CATEGORY IV for this route of exposure when used as a SAR inducer.

Skin Sensitization (OPPTS Guideline 870.2600; MRID Nos. 47264935 and 47264978): Data indicate Laminarin is not a dermal sensitizer. However, any reported incidents may cause this position to be reconsidered.

Subchronic Testing (OPPTS Guideline 870.3100, 870.3250, 870.3465; MRID Nos. 47264937, 47264938 and 47264939): In accordance with footnote seven and eight in the Biochemical Pesticides Human Health Assessment Data Requirements table in 40 CFR § 158.2050, subchronic dermal and subchronic inhalation testing were not required for a lack of exposure. Three subchronic oral tests were submitted in support of Laminarin's food use. These studies satisfy the data requirement for subchronic oral testing and indicate that Laminarin has no subchronic toxicological effect through the oral route of exposure. A 28-day oral toxicity study found no toxicological effects regarding mortality, clinical observations, neurotoxicity assessment, body weight, food consumption, hematology, clinical chemistry, organ weights, and macroscopic or microscopic observations. The NOEL was determined to be 1,000 mg/kg/day. A 90-day oral toxicity study found no statistical difference in hematology, clinical chemistry, or urinalysis between test subjects and the control. The NOEL was determined to be 1,000 mg/kg/day. Another 90-day oral toxicity study also found no statistical difference in hematology, clinical chemistry, or urinalysis between test subjects and the control. And the NOEL was again determined to be 1,000 mg/kg/day. All subchronic oral toxicity studies indicate that Laminarin is not subchronically toxic through the oral route of exposure.

Developmental Toxicity (OPPTS Guideline 870.3700; MRID Nos. 47264940 and 47264941): Data submitted to the Agency satisfy the data requirement and support the Agency's conclusion that there is no risk of developmental toxicity associated with the new food uses. A prenatal developmental toxicity study on rats found no significant reproductive effects or fetal abnormalities, and established a NOAEL of 1,000 mg/kg/day. The findings suggest negligible risk with regard to developmental toxicity.

Mutagenicity Testing (OPPTS Guidelines 870.5100, 870.5300, 870.5375; MRID Nos. 47264942, 4726493 and 47264944): Three genotoxicity studies (a Bacterial Reverse Mutation Test, and an *In Vitro* Mammalian Cells in Culture Assay) were performed on the active ingredient Laminarin and satisfy the data requirement. The Reverse Mutation Assay showed that Laminarin did not induce mutant colonies over expected background levels. The *In Vitro* Mammalian Cells in Culture Assay demonstrated that Laminarin did not damage chromosomes or the mitotic apparatus of bone marrow cells. These mutagenicity studies are sufficient to confirm that there are no expected dietary, occupational, or non-occupational risks of mutagenicity with regard to Laminarin.

b. Acute Toxicity – Tier II and Tier III (40 CFR § 158.2050)

The Tier II studies listed below were the only higher Tier studies required for Laminarin. No other studies were required based on a lack of acute toxicity in the Tier I studies and a lack of exposure relative to its use pattern as a SAR inducer

Developmental Toxicity (OPPTS Guideline 870.3700; MRID No. 47264941): Tier II data are required on the active ingredient for developmental toxicity if there might be regular exposure to women. In that case, a second prenatal study using a different test subject is required. A second prenatal developmental toxicity study on rabbits found no significant treatment-related reproductive effects or fetal abnormalities, and confirmed a NOAEL of 1,000 mg/kg/day. Data submitted to the Agency confirm that Laminarin poses negligible risk with regard to developmental toxicity.

Mutagenicity Testing (OPPTS Guidelines 870.5385; MRID No. 47264944): Tier II data are required on the active ingredient for mutagenicity testing for the active ingredient. A bone Marrow Micronucleus Assay indicated that no toxicity was noted in either sex at any dose up to the limit dose of 2000 mg/kg. This mutagenicity study, in conjunction with the Tier I mutagenicity studies, satisfies the data requirement for mutagenicity testing and is sufficient to confirm that there are no expected dietary, occupational, or non-occupational risks of mutagenicity with regard to Laminarin.

Immunotoxicity Testing (OPPTS Guidelines 880.3550; MRID No. 47264945): A waiver request was accepted for immunotoxicity for the following reasons: 1) The potential for any immunotoxic effect is precluded by the Laminarin's biodegradability. 2) Laminarin is not structurally related to any known immunotoxic chemical. 3) There is a long history of the consumption of Laminarin without known immunotoxicological incident. 4) The toxicological profile in acute toxicological studies, subchronic studies and developmental studies does not suggest any immunotoxicity. All information points to the lack of dietary risk posed by the immunotoxicity of Laminarin residues, and supports the exemption from the requirement of a tolerance.

c. Effects on the Endocrine System

EPA is in the process of issuing test orders for endocrine effects. The schedule for issuance of test orders, and details regarding status is available at http://www.epa.gov/endo/. EPA has also established a docket for the test orders in www.regulations.gov under docket number EPA-HQ-OPP-2009-0634.

Data required under the test orders will provide information to help EPA identify whether chemicals have the potential to interact with the estrogen, androgen, and/or thyroid hormone systems, which regulate growth, metabolism, development, and reproduction. The data generated from the screens will provide robust and systematic scientific information that will help EPA identify whether additional testing is necessary.

Laminarin is a naturally occurring carbohydrate present in our fruits and vegetables. To date, there is no evidence to suggest that our natural exposure to Laminarin affects the immune system, functions in a manner similar to any known hormone, or that it acts as an endocrine

disruptor. Moreover, the use of Laminarin is not expected to result in any significant exposures, effectively obviating any opportunity for negative effects on humans or the environment. Therefore, it is unlikely that Laminarin will have estrogenic or endocrine effects.
Because there is no available evidence demonstrating that Laminarin is an endocrine disruptor, the Agency is not requiring information on the endocrine effects of Laminarin at this time. However, the Endocrine Disruption Screening Program (EDSP) has established a protocol, which guides the Agency in selecting suspect ingredients for review; and the Agency reserves the right to require new information, should the program require it. Presently, based on the lack of exposure and the negligible toxicity profile of the extract, no adverse effects to the endocrine or immune systems are known or expected.

2. Dose Response Assessment

No toxicological endpoints were identified; therefore, a dose response assessment was not required.

3. Dietary Exposure and Risk Characterization

Exposure to residues of Laminarin on foods is expected to be negligible; and even in the event of dietary exposure, no dietary risks are anticipated. Data submitted to the Agency show that Laminarin is 65% to 71% biodegraded within two weeks, and that it hydrolyzes very rapidly into glucose. Because applications tend to occur earlier in the growing season (due to its mode of action as a SAR inducer), and given its short-lived presence on crops, no significant pesticidal residues are anticipated for harvested foods. Even in the event of exposure to residues, however, no dietary risks are anticipated. Acute, subchronic, and teratogenicity studies support its non-toxic profile. It is already present in the human diet – especially in cereal grains - without any known detrimental effect. Furthermore, it is approved by US FDA as a food additive, a dietary supplement and a texturing agent in processed foods in quantities greater than any expected pesticidal residues. There is no information in the public literature suggesting any health issues to either animals or plants relative to this compound. In sum, no dietary exposure is expected; and any potential dietary exposures would not be expected to pose any quantifiable risk, due to its nontoxic profile.

4. Drinking Water Exposure Risk Characterization

Residues of Laminarin are not expected to be present in drinking water. Applications of Laminarin are made directly to terrestrial crops. These residues biodegrade rapidly, and are not expected to percolate through soil. Even in the event of an errant spray drift or an extraordinary rainfall event, Laminarin does not persist in water due to its rapid hydrolyzation into glucose. Moreover, risks from a miniscule aquatic exposure would be negligible, given Laminarin's nontoxic profile. Altogether, drinking water exposure is not expected to pose any quantifiable risk due to a lack of residues, and the nontoxicity of Laminarin.

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

Dietary exposure to humans, including infants and children, are considered negligible with regard to the pesticidal use of Laminarin. Because Laminarin is mostly biodegraded within two weeks and applications of Laminarin tend to occur earlier in the growing season with a minimum of ten day intervals between applications, no significant residues of Laminarin are expected on foods. Additionally, Laminarin is known to hydrolyze in water relatively rapidly, and so what few residues might exist at harvest would be degraded into glucose during processing. In the event that there are any residues, acute toxicity studies indicate that Laminarin has negligible toxicity. It is ubiquitous in nature and present in all edible plants, and there is no history of toxicological incident involving its consumption. Its use is approved by FDA as a food additive, a dietary supplement and as a texturing agent for processed foods. While no dietary exposures are expected, the Agency has determined there is a reasonable certainty of no harm to the general US population, including infants and children, from exposure to this active ingredient.

6. Occupational, Residential, School and Day Care Exposure and Risk Characterization

As an agricultural pesticide, some occupational exposure to Laminarin can reasonably be expected. Such occupational exposures are expected to be insignificant because - by virtue of Laminarin's mode of action as a SAR inducer - applications are directed and infrequent. The insignificance of any exposure is even more pronounced for residential, school, or daycare areas. Even in the event of incidental exposure, health risks to humans, including infants and children, are considered negligible, given Laminarin's nontoxic profile.

a. Occupational Exposure and Risk Characterization

Occupational exposures are expected to be minimal. As a biochemical with a preventative mode of action, applications of Laminarin will tend to be limited to early in the growing season when it can best bolster plant defenses; and applications are expected to occur at more infrequent intervals than most other pesticides, as SAR induction requires time to be actualized in the plants. Also, foliar applications are expected for the substance to be most effective, further diminishing the chance of spray drift associated with area-wide sprays. Regardless, requirements for the use of appropriate personal protective equipment and precautionary statements are required on product labels to mitigate any potential risks to pesticide handlers due to prolonged exposure. But, even in the event of occupational exposure, any health risks associated with regular exposure seem unlikely. Humans have long consumed Laminarin in fruits and vegetables with no history of detrimental effects. Moreover, Laminarin has been approved by FDA as a food additive and for use in ointments, suggesting a lack of risks for both the oral and the dermal routes of exposure. And with regard to pesticidal applications, all acute, subchronic, and developmental toxicity data submitted in support of this application for Laminarin confirm its lack of toxicity through all routes of exposure. Because of a lack of likely exposure to

residues and a well established nontoxic profile for Laminarin, no occupational risks are expected with regard to the use of this active ingredient.

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

The Agency does not expect any risks to children (or adults) in any of these environments. Due to the agricultural use pattern of Laminarin, the potential for significant exposure is negligible. Even in the remote event of incidental residue, the active ingredient has a nontoxic profile for all routes of exposure and a long history of consumption without incident. Due to limited exposure scenarios and negligible toxicity hazards, no risks are expected relative to these exposure scenarios.

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

The potential for aggregate exposure is expected to be insignificant. Directed Laminarin spray is not expected to result in significant amounts of respirable mist, and is not anticipated to be in non-occupational environments at all. Likewise directed foliar applications, are not likely to result in dermal exposures, especially in non-occupational environments. The chance of significant incidental residues, which could be consumed are also slight. Given a lack of any significant non-occupational exposure, a lack of concern regarding its naturally occurring background levels, and a lack of any acute toxicological endpoints for Laminarin, the aggregate exposure scenario presents no significant concerns for risk.

8. Cumulative Effects

Pursuant to FFDCA section 408(b)(2)(D)(v), EPA has considered available information concerning the cumulative effects of Laminarin residues and other substances that have a common mechanism of toxicity. These considerations include the potential for cumulative effects on infants and children of Laminarin residues and other substances with a common mechanism of toxicity. Because Laminarin has a long history of dietary consumption without incident, and because no toxicological endpoints have been established, the Agency concludes that Laminarin does not share a common mechanism of toxicity, and that there are no cumulative effects arising from Laminarin residues in or on food commodities.

9. Risk Characterization

The Agency considered human exposure to Laminarin in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of Laminarin when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Hazards (Relative to the Biochemical Pesticides Nontarget Organisms and Environmental Fate Data Requirements - 40 CFR § 158.2060)

Non-target organism and environmental fate data requirements were satisfied by submission of studies. Laminarin is known to occur naturally in the terrestrial and aquatic environment, and is not associated with any known detrimental effect. All information available to the Agency validates a non-toxic mode of action, a lack of persistence in the environment, and a lack of adverse effects relative to non-target organisms.

In accordance with T-REX Model and the non-target data submitted, the Agency has made a "No Effect" (NE) determination for direct and indirect effects to any listed threatened and endangered species and their habitat as a result of the proposed uses of Laminarin.

Avian Testing (OPPTS Guidelines 850.2100, 850.2200; MRID Nos. 47264950 and 47264951): No avian toxicity is expected with regard to the pesticidal use of Laminarin. In an acute oral toxicity study, groups of bobwhites were administered single oral doses ranging up to 2000 mg/kg body weight Laminarin. They were observed for 14 days. There were no mortalities and no signs of adverse effects - all birds appeared healthy during the test, and macroscopic examination revealed no abnormalities in any birds. The acute oral LD_{50} was >2000 mg/kg, the highest dose tested. In a dietary toxicity study on bobwhites, groups of chicks were provided a Laminarin-dosed diet for 5 days, at concentrations ranging up to 5000 ppm per feeding. The diet was maintained for 5 days. There were no treatment-related effects on mortality, body weight, or feed consumption, and no clinical signs of toxicity. The dietary LD_{50} was determined to be >5000 ppm. A lack of toxicological endpoints supports the conclusion that Laminarin is nontoxic to birds.

Aquatic Organism Testing (OPPTS Guidelines 850.1010, 850.1075, 850.5400; MRID Nos. 47264947, 47264948, 47264949, and 47264953): No risks are expected with regard to the exposure of aquatic organisms to Laminarin. Aquatic exposure is unlikely due to the rapid biodegradation and hydrolysis of Laminarin. But in the event of aquatic exposures, no hazards are expected for aquatic organisms. In an acute toxicity test, groups of *Daphnia magna* were exposed to concentrations of Laminarin up to 100 mg/L Laminarin. No daphnid mortality or immobility was seen in any of the test groups after 24 or 48 hours. In this study, the 48-hr NOEC and EC_0 were each ≥100 mg/L, and the LOEC and EC_{50} were >100 mg/L. In an acute toxicity test, groups of zebrafish were exposed to a nominal concentration of 0 or 100 mg/L Laminarin for 96 hours. No mortality or adverse clinical signs were seen at any intervals or in any of the test groups. The 96-hr LC_{50} for Laminarin in Zebra Fish was >100 mg/L. In a second toxicity test, groups of Rainbow Trout fry were exposed to a nominal concentration of 0 or 100 mg/L Laminarin for 96 hours. No mortality or adverse clinical signs were seen in any of the test groups. The 96-hr LC_{50} for Laminarin in Rainbow Trout was >100 mg/L. A 72-hour laboratory

study was conducted to determine the effects of Laminarin (100 mg/L, nominal) on the growth of the unicellular freshwater green algae. An untreated control was also included in the test. At test end, cell growth and density were similar in the test material and control group. The 72-hour EbC_{50} and ErC_{50} for H11 were >100 mg/L, and the NOECb and NOECr were >100 mg/L. The 4 studies altogether confirm a lack of toxicological endpoints, and indicate that Laminarin is nontoxic to aquatic organisms

Non-Target Plant Testing (OPPTS Guidelines 850.4100, 850.4150): The data requirement was satisfied by information demonstrating a lack of hazard to non-target plants relative to the active ingredient's mode of action. The active ingredient is to be directed at agricultural crops; incidental residues would be negligible. To the degree that there is incidental exposure, Laminarin has been shown to have a non-toxic mode of action relative to plants. As a SAR inducer, Laminarin bolsters plant health. Accordingly, Laminarin would actually be expected to have a strengthening effect on non-target plants.

Non-Target Insect Testing (OPPTS Guideline 880.4350, 850.3020); MRID Nos. 47264979 and 47264952): Data indicate that the residues of Laminarin pose no risks of toxicity to non-target insects. In a laboratory study, groups of male and female adult parasitic wasps were exposed for 48 hours to 37 g/L Laminarin sprayed on glass plates at varying rates up to10.0 L/ha. Some issues of loss of fecundity were observed at the highest dose; but none were observed at the doses that were in line with the expected applications of the active ingredient. (The dose at which there was a loss of fecundity was 10x greater than expected residues of Laminarin at the time of pesticidal application.) There was no statistically significant difference in mortality between the treated wasps and the untreated control groups. Limit tests were conducted to determine the acute oral and acute contact toxicity of Laminarin to the Honey Bee. Both tests used a nominal dose of 100.00 µg Laminarin/bee. In the oral toxicity test, groups of caged bees were provided the test material in a 50% w/v sucrose solution for six hours, and then monitored for mortality at intervals up to 48 hours. After 48 hours, there was no difference in mortality of the untreated control and test material groups. In the contact toxicity test, bees were anesthetized with carbon dioxide and received an individual application of Laminarin to the ventral thorax. In this test, the 48-hr oral toxicity LD_{50} for Laminarin was >118.64 µg/bee, and the 48-hr contact toxicity LD_{50} was >100.00 µg/bee. Data indicate that exposures to Laminarin are not expected to result in any adverse effects to non-target insects.

2. Environmental Fate and Ground Water Data

The need for environmental fate and groundwater data was not triggered because results of the acute toxicity assessment did not trigger any additional Tier I studies.

3. Ecological Exposure and Risk Characterization

The use of Laminarin is not expected to result in significant ecological exposures; and to the degree that there are any incidental exposures, all data on file with the Agency demonstrate that

Laminarin is nontoxic to non-target organisms. Laminarin is intended to be applied directly to crops early in the growing season at bi-monthly intervals. Biodegradability data show that it does not persist, and that it hydrolyzes rapidly. (Laminarin is 65-71% biodegraded within two weeks.) When used according to the proposed label directions, no direct exposures are expected for non-target organisms. Laminarin is a naturally occurring carbohydrate. Its presence in the environment has no known toxicological effect on animals or plants. Data submitted to satisfy the non-target organism data requirements confirm Laminarin's lack of ecotoxicity. No adverse effects were observed on plants, insects, mammals, avian species and aquatic organisms; and no toxicological endpoints were identified for any of these organisms. No risks are expected to the environment with regard to the pesticidal use of Laminarin.

4. Threatened and Endangered Species Assessment

Based on the available data, a **No Effects (NE)** determination was made for Laminarin on threatened and endangered species when Laminarin is applied to crops as a SAR inducer. The Agency notes that all non-target organism data indicate no toxicity to non-target organisms. Laminarin has a non-toxic mode of action, which precludes toxic effects on plants. And Laminarin is intended to be applied as an agricultural product; accordingly exposures to threatened and endangered species are expected to be negligible. The Agency used its T-REX Model and its Individual Effects Chance Model Version 1.1, in conjunction with data submitted on non-target organisms to quantifiably estimate the chance of risk to endangered/threatened avian and aquatic species from exposure to Laminarin. These values (avian risk at 1 in 294,000 and aquatic risk at 1 in 418,000,000) suggest that Laminarin should not cause toxic risk to endangered/threatened species. The calculated RQ values for endangered/threatened terrestrial (RQ = 0.00) and aquatic species (RQ = 0.0045) are below the Agency's LOCs of 0.1 and 0.5, respectively, supporting the Agency's finding that exposure to Laminarin will have **No Effect (NE)** on threatened and endangered species.

V. ENVIRONMENTAL JUSTICE

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to Laminarin, compared to the general population. Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

VI. RISK MANAGEMENT AND REGISTRATION DECISIONS

A. Determination of Eligibility

Section 3(c)(5) of FIFRA provides for the registration of new active ingredients if it is determined that (A) its composition is such as to warrant the proposed claims for it; (B) its labeling and other materials required to be submitted comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.

The four criteria of the Eligibility Determination for Pesticidal Active Ingredients are satisfied by the science assessments supporting products containing Laminarin. Such products are not expected to cause unreasonable adverse effects, and are likely to provide protection as claimed when used according to label instructions. Therefore, EPA concludes that Laminarin is eligible for registration for the labeled uses.

B. Regulatory Decision

On October 1, 2009, EPA announced a new policy to provide a more meaningful opportunity for the public to participate on major registration decisions before they occur. According to this new policy, EPA intends to provide a public comment period prior to making a registration decision for, at minimum, the following types of applications: new active ingredients; first food use; first outdoor use; first residential use; and other actions for which the Agency anticipates significant public interest. Accordingly, this pesticide was subject to a 30-day comment period as a new active ingredient with both food uses and outdoor uses. No comments were received during that comment period.

At this time, EPA believes, the data submitted fulfill the requirements of registration for products containing Laminarin for use as a SAR inducer. Acute toxicity data for Laminarin demonstrate that it is toxicity category III and IV for all routes of exposure. (No toxicological endpoints were established.) Data confirm that Laminarin does not demonstrate subchronic or developmental toxicity, and it is not mutagenic or genotoxic. EPA has no concerns for any non-target organisms exposed to Laminarin in accordance with its approved uses. EPA has not identified any toxic endpoints for non-target mammals, birds, plants, aquatic, or soil organisms; nor are there concerns for any threatened and endangered species. Given, the non-toxic character of Laminarin, EPA supports its registration under Section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Refer to Appendix B for product-specific information.

1. Conditional/Unconditional Registration

All data requirements are fulfilled and EPA has determined that an unconditional registration for Laminarin is warranted under Section 3(c)(5) of FIFRA.

C. Labeling

Before releasing pesticide products containing Laminarin for shipment, the applicant is required to provide appropriate labels.

VII. ACTIONS REQUIRED BY THE REGISTRANT

The Agency evaluated the data submitted in connection with the initial registration of Laminarin and determined that these data fulfill current registration guideline requirements. No additional data are required to be submitted to the Agency at this time. Additional data may be required for new uses and/or changes to existing uses.

Not withstanding 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 and Hypersensitivity Incidents

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).

Additionally, all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency under the provisions of 40 CFR Part 158.2140 OPPTS Guideline reference number 885.3400.

VIII. GLOSSARY OF ACRONYMS AND ABBREVIATIONS

BPPD	Biopesticides and Pollution Prevention Division
BRAD	Biopesticide Registration Action Document
CFR	Code of Federal Regulations
cm^3	cubic centimeter
CSF	Confidential Statement of Formula
°C	degrees Celsius
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
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
LD_{50}	median lethal dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, or inhalation). It is expressed as a weight of substance per unit weight of animal (e.g., mg/kg).
MRID No.	Master Record Identification Number
mg	milligram
mL	milliliter
MP	manufacturing-use product
MPCA	microbial pest control agent
NE	"No Effect"
NIOSH	National Institute for Occupational Safety and Health
OPP	Office of Pesticide Programs
OPPTS	Office of Prevention, Pesticides, and Toxic Substances
PCR	polymerase chain reaction
PPE	personal protective equipment
TGAI	technical grade of the active ingredient

IX. BIBLIOGRAPHY STUDIES SUBMITTED IN SUPPORT OF THIS REGISTRATION

A. Studies Submitted in Support of this Registration.

MRID	Citation	Receipt Date
47264900	Laboratoires Goemar S.A. (2007) Submission of Efficacy, Toxicity and Product Chemistry Data in Support of the Application for Registration of Vacciplant. Transmittal of 78 Studies.	24-Oct-2007
47264901	Smith, F. (2007) Product Identity and Composition, Description of Beginning Material, Manufacturing Process, and Discussion of Formation of Impurities: (Vacciplant). Unpublished study prepared by SciReg, Inc. 18 p.	24-Oct-2007
47264902	Trebert, R. (2001) Laminarin - Analytical Profiles of Batches: (Final Report). Project Number: BPL/200007/0395. Unpublished study prepared by Crepin Analyses & Controles. 84 p.	24-Oct-2007
47264904	Cruz, F. (1998) Determination of Pure Laminarin: Global Method. Project Number: FC98005. Unpublished study prepared by Laboratories GOEMAR. 8 p.	24-Oct-2007
47264905	Trebert, R.; Cousin, C. (2002) Validation of the Method of the Dosage of Pure Laminarin: Global Method: (Final Report). Project Number: BPL/200107/1309. Unpublished study prepared by Crepin Analyses & Controles. 27 p.	24-Oct-2007
47264906	Delolme, F. (2007) Analysis by MALDI-TOF Mass Spectrometry. Project Number:	24-Oct-

	FC000828. Unpublished study prepared by SciReg, Inc. 7 p.	2007
47264907	Smith, F. (2007) Summary of the OPPTS 830 Series Physical-Chemical Properties Test Guidelines: (Vacciplant). Unpublished study prepared by SciReg, Inc. 15 p.	24-Oct-2007
47264908	Smith, F. (2007) Color, Odor, Physical State: (Vacciplant). Unpublished study prepared by SciReg, Inc. 4 p.	24-Oct-2007
47264909	Trebert, R. (2002) G.L.P. Stability Study on Laminarin Code H 11 Batch N S012000 According to EPA 830.6313: Final Report. Project Number: BPL/200112/0368. Unpublished study prepared by Crepin Analyses & Controles. 31 p.	24-Oct-2007
47264910	Cuthbert, J. (2001) Laminarin: Determination of Spectra. Project Number: 1476/001VM. Unpublished study prepared by Safepharm Laboratories, Ltd. 24 p.	24-Oct-2007
47264911	Luc, L. (2000) Laminarin-Oxidizing Properties. Project Number: 00/907005/020. Unpublished study prepared by SEPC. 23 p.	24-Oct-2007
47264912	Luc, L. (2007) Laminarin- Flammability of Solids. Project Number: 00/907005/016. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264913	Luc, L. (2000) Laminarin-Self-Ignition Temperature of Solids. Project Number: 00/907005/019. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264914	Luc, L. (2000) Laminarin-Flammability in Contact with Water. Project Number: 00/907005/017. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264915	Luc, L. (2000) Laminarin-Explosive Properties (Solid). Project Number: 00/907005/018. Unpublished study prepared by SEPC. 25 p.	24-Oct-2007
47264916	Luc, L. (2000) Laminarin-Melting Point. Project Number: 00/907005/003. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264917	Luc, L. (2000) Laminarin - Relative Density. Project Number: 00/907005/005. Unpublished study prepared by SEPC. 21 p.	24-Oct-2007
47264918	Claude, A. (2002) Laminarin-Relative Density. Project Number: 01/907005/002. Unpublished study prepared by SEPC. 21 p.	24-Oct-2007
47264919	Luc, L. (2002) Laminarin - Soulubility in Water. Project Number: 00/907005/008. Unpublished study prepared by SEPC. 43 p.	24-Oct-2007
47264920	Martel, I. (2002) Determination of pH Values - (Laminarin). Project Number: 01/907005/001. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264921	Luc, L. (2001) Laminarin-Solubility in n-Heptane. Project Number: 00/907005/09, SEP/00/068. Unpublished study prepared by SEPC. 41 p.	24-Oct-2007
47264922	Luc, L. (2001) Laminarin - Solubility in Xylene. Project Number: 00/907005/010, SEP/00/069. Unpublished study prepared by SEPC. 41 p.	24-Oct-2007
47264923	Luc, L. (2001) Laminarin-Solubility in 1,2 Dichloroethane. Project Number:	24-Oct-

	00/907005/011, SEP/00/070. Unpublished study prepared by SEPC. 41 p.	2007
47264924	Luc, L. (2001) Laminarin-Solubility in Methanol. Project Number: 00/907005/012, SEP/00/071. Unpublished study prepared by SEPC. 41 p.	24-Oct-2007
47264925	Luc, L. (2001) Laminarin-Solubility in Acetone. Project Number: 00/907005/013, SEP/00/072. Unpublished study prepared by SEPC. 41 p.	24-Oct-2007
47264926	Luc, L. (2001) Laminarin-Solubility in Ethyl Acetate. Project Number: 00/907005/014, SEP/00/073. Unpublished study prepared by SEPC. 41 p.	24-Oct-2007
47264927	Tremain, S. (2001) Laminarin: Determination of Vapour Pressure. Project Number: 1303/005. Unpublished study prepared by Safepharm Laboratories, Ltd. and SEPC. 21 p.	24-Oct-2007
47264928	Quintelas, G. (2001) Determination of the Partition Coefficient of Laminarin. Project Number: SEP/00/074, 00/907005/015. Unpublished study prepared by Defitraces. 25 p.	24-Oct-2007
47264929	Luc, L. (2000) Laminarin-Surface Tension. Project Number: 00/907005/007. Unpublished study prepared by SEPC. 19 p.	24-Oct-2007
47264930	Baudet, L. (2002) Phycarine 96S51: Acute Toxicity Study Safety Test in the Rat by the Oral Route. Project Number: 20010618/ST. Unpublished study prepared by Centre de Recherches Biologiques. 27 p.	24-Oct-2007
47264931	Audeval Gerald, C. (2001) H11 (Batch 99S24) Acute Dermal Toxicity Study in the Rat. Project Number: 20000698/ST, 20000698/ST/TAUVD/H11. Unpublished study prepared by Centre de Recherches Biologiques. 30 p.	24-Oct-2007
47264932	Muller, W. (1999) Evaluation of Acute Inhalation Toxicity with Phycarine in Rats. Project Number: 980001/EX, TOXLABS/1998/7019/INH. Unpublished study prepared by Centre de Recherches Biologiques. 19 p.	24-Oct-2007
47264933	Baudet, L. (2002) Phycarine 96S51: Ocular Primary Irritation in the Rabbit. Project Number: 20010615/ST. Unpublished study prepared by Centre de Recherches Biologiques. 27 p.	24-Oct-2007
47264934	Baudet, L. (2002) Phycarine 96S51: Cutaneous Primary Irritation in the Rabbit: Final Report. Project Number: 20010617/ST/PSI/RABBIT/PHYCARIINE. Unpublished study prepared by Centre de Recherches Biologiques. 25 p.	24-Oct-2007
47264935	Baudet, L. (2002) Phycarine 96S51: Study of Cutaneous Sensitization Using the Magnusson and Kligman Maximisation Test in the Guinea Pig: Final Report. Project Number: 20010616/ST. Unpublished study prepared by Centre de Recherches Biologiques. 39 p.	24-Oct-2007
47264936	Delille, M. (1998) Acute Toxicity Study: Safety Test in the Rat by the Subcutaneous Route: (Phycarine 96S51). Project Number: 970353/ST. Unpublished study prepared by Centre de Recherches Biologiques. 24 p.	24-Oct-2007
47264937	Longobardi, C. (2000) 4489-1 (product H 11): 4 Week Oral Toxicity Study in Rats: Final Report. Project Number: 7286, 7286/T/240/99. Unpublished study prepared by Research Toxicology Centre, S.p.A.. 178 p.	24-Oct-2007

47264938	Audeval Gerard, C. (2001) H11 (Batch 99S24): 90-Day Repeated Dose Oral Toxicity Study in the Rat. Project Number: 20000389/T. Unpublished study prepared by Centre de Recherches Biologiques. 237 p.	24-Oct-2007
47264939	Audeval Gerard, C. (2001) 90-Day Repeated Dose Oral Toxicity Study in the Dog. Project Number: 20000390/T. Unpublished study prepared by Centre de Recherches Biologiques. 257 p.	24-Oct-2007
47264940	Audeval Gerard, C. (2001) H11 (Batch 99S24): Study for the Effects on Embryo-Foetal Development in the Rat by the Oral Route. Project Number: 20000387/T. Unpublished study prepared by Centre de Recherches Biologiques. 127 p.	24-Oct-2007
47264941	Gerard, C. (2001) Study for the Effects on Embryo-Foetal Development in the Rabbit by the Oral Route: H11 (Batch 99S24). Project Number: NO/20000388/T. Unpublished study prepared by CERB (Centre de Recherches Biologiques). 127 p.	24-Oct-2007
47264942	Marzin, D. (2000) Mutagenicity Test on Bacteria (Salmonella typhimurium his and Escherichia coli trp) Using B.N. Ames's Technique with H11. Project Number: IPL/R/991011/H11/GOEMAR/LABORATORY. Unpublished study prepared by Institut Pasteur de Lille. 38 p.	24-Oct-2007
47264943	Haddouk, H. (2002) In Vitro Mammalian Cell Gene Mutation Test in L5178Y TK Mouse Lymphoma Cells: Laminarin. Project Number: 22626/MLY. Unpublished study prepared by Centre International de Toxicologie. 47 p.	24-Oct-2007
47264944	Haddouk, H. (2001) Bone Marrow Micronucleus Test by Oral Route in Mice: Laminarin. Project Number: 21149/MAS, 21149/MAS/LAMINARIN/LABORATOIRES/GOEMAR/SA. Unpublished study prepared by Centre International de Toxicologie. 37 p.	24-Oct-2007
47264945	Smith, F. (2007) Toxicology Waiver Request - Immunotoxicity (Laminarin). Unpublished study prepared by SciReg, Inc. 11 p.	24-Oct-2007
47264946	Quintelas, G. (2001) Abiotic Degradation of Laminarin pH Dependent Hydrolysis (Test C7). Project Number: SEP/00/075, SEPC/00/907005/025, 00/907005/025. Unpublished study prepared by Defitraces. 30 p.	24-Oct-2007
47264947	Herti, J. (2001) Acute Toxicity of Laminarin to Daphnia magna in a 48-Hour Semi-Static Immobilization Test: Final Report. Project Number: PROJECT/10041220. Unpublished study prepared by Institut fuer Biologische Analytik und Consulting IBACON. 61 p.	24-Oct-2007
47264948	Luc, L. (2001) Acute Toxicity in Freshwater Fish (96h): Oncorhynchus mykiss (Laminarin). Project Number: 00/907005/021. Unpublished study prepared by SEPC. 50 p.	24-Oct-2007
47264949	Luc, L. (2001) Acute Toxicity in Freshwater Fish (96h): Danio rerio: (Laminarin). Project Number: 00/907005/022. Unpublished study prepared by SEPC. 49 p.	24-Oct-2007
47264950	Rodgers, M. (2002) Laminarin: Acute Oral Toxicity (LD50) to the Bobwhite Quail. Project Number: GOM/001, GOM/001/022173. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 23 p.	24-Oct-2007

47264951	Rodgers, M. (2002) Laminarin: Dietary Toxicity (LC50) to the Bobwhite Quail. Project Number: GOM/002, GOM/002/014410. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 21 p.	24-Oct-2007
47264952	Kling, A. (2000) Assessment of Side Effects of Laminarin to the Honey Bee, Apis mellifera L. in the Laboratory: Final Report. Project Number: 20001342/01/BLEU. Unpublished study prepared by Arbeitsgemeinschaft GAB Biotechnologie. 33 p.	24-Oct-2007
47264953	Gnemi, P. (2000) H11: Algal Growth Inhibition Study. Project Number: 990714. Unpublished study prepared by Istituto di Ricerche Biomediche Antoine Marxer RBM S.p.A. 27 p.	24-Oct-2007
47264954	Luc, L. (2000) Ready Biodegradability Modified Strum Test: (Laminarin). Project Number: 00/907005/024. Unpublished study prepared by SEPC. 24 p.	24-Oct-2007
47264955	Smith, F. (2007) Product Identity and Composition, Description of Beginning Materials, Description of Formulation Process, Discussion of Formation of Impurities, and Certified Limits (Vacciplant). Unpublished study prepared by SciReg, Inc. 57 p.	24-Oct-2007
47264956	Smith, F. (2007) Summary of the OPPTS 830 Series Physical-Chemical Properties Test Guidelines (Vacciplant). Unpublished study prepared by SciReg, Inc. 6 p.	24-Oct-2007
47264957	Luc, L. (2001) Phyliq: Determination of pH Value of the Test Item . Project Number: 00/907005/026. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264958	Luc, L. (2001) Phyliq: Determination of pH Value of a 1% Aqueous Dilution. Project Number: 00/907005/028. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264959	Luc, L. (2001) Phyliq: Determination of pH Value of the Test Item After an Accelerated Storage Procedure at + 54 Degrees Celsius for 14 Days. Project Number: 00/907005/035. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264960	Luc, L. (2001) Phyliq: Determination of pH Value of a 1% Aqueous Dilution After an Accelerated Storage Procedure at + 54 Degrees Celsius for 14 Days. Project Number: 00/907005/037. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264961	Luc, L. (2001) Phyliq: Viscosity. Project Number: 00/907005/029. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264962	Luc, L. (2001) Phyliq: Relative Density. Project Number: 00/907005/030. Unpublished study prepared by SEPC. 20 p.	24-Oct-2007
47264963	Luc, L. (2001) Phyliq: Storage Stability: Accelerated Procedure by Heating (at +54 Degrees Celsius for 14 Days). Project Number: 00/907005/034. Unpublished study prepared by SEPC. 39 p.	24-Oct-2007
47264965	Luc, L. (2001) Phyliq: Low Temperature Stability. Project Number: 00/907005/040. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264966	Luc, L. (2001) Phyliq: Dilution Stability. Project Number: 00/907005/033. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007

47264967	Luc, L. (2001) Phyliq: Dilution Stability After an Accelerated Storage Procedure at +54 (Degrees) Celcius for 14 Days. Project Number: 00/907005/039. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264968	Luc, L. (2001) Phyliq: Surface Tension. Project Number: 00/907005/031. Unpublished study prepared by SEPC. 20 p.	24-Oct-2007
47264969	Luc, L. (2001) Phyliq: Persistent Foaming. Project Number: 00/907005/032. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264970	Luc, L. (2001) Phyliq: Persistent Foaming After an Accelerated Storage Procedure at +54 Degrees Celcius for 14 days. Project Number 00/907005/038. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264971	Luc, L. (2001) Phyliq: Free Acidity or Alkalinity. Project Number: 00/907005/027. Unpublished study prepared by SEPC. 18 p.	24-Oct-2007
47264972	Luc, L. (2001) Free Acidity or Alkalinity After an Accelerated Storage Procedure at + 54 C for 14 Days. Project Number: 00/907005/036. Unpublished study prepared by SEPC. 17 p.	24-Oct-2007
47264973	Audeval-Gerard, C. (2000) Acute Oral Toxicity Study in the Rat. Project Number 9912812, 990762T/Limvo/Phyliq. 27 p.	24-Oct-2007
47264974	Audeval-Gerard, C. (2000) Acute Dermal Toxicity in the Rat. Project Number 9912812, 990763T/LIMVD/PHYLIQ. 28 p.	24-Oct-2007
47264975	Smith, F. (2007) Toxicology Waiver Request - Acute Inhalation Toxicity: (Laminarin). Project Number: TOXLABS/1998/7020INH, 24634/61/5. Unpublished study prepared by SciReg, Inc. 81 p.	24-Oct-2007
47264976	Audeval-Gerard, C. (2000) Acute Eye Irritation Study in the Rabbit. Project Number: 990760T/IPOCH/PHYLIQ, 9912812. Unpublished study prepared by Laboratories Goemar SA. 27 p.	24-Oct-2007
47264977	Audeval-Gerard, C. (2000) Acute Skin Irritation Study in the Rabbit. Project Number: 9912812, 990759T/IPCCH/PHYLIQ. Unpublished study prepared by Laboratories GOEMAR SA. 27 p.	24-Oct-2007
47264978	Audeval-Gerard, C. (2000) Skin Sensitisation Study in the Guinea Pig (Magnusson-Kligman Maximisation). Project Number: 990761/KINJCH/PHYLIQ, 9912812. Unpublished study prepared by Laboratories GOEMAR SA. 37 p.	24-Oct-2007
47264979	Tessier, C. (2001) The Effects of Phyliq (37 g/L Laminarin) on Aphidius rhopalosiphi (Hymenoptera, Braconidae) on Artificial Substrate in Laboratory: LR 50 Estimation and Reproduction Assessment: Phyliq. Project Number: 01APGOL25. Unpublished study prepared by Promo-Vert S.A. 18 p.	24-Oct-2007
47264980	Tessier, C. (2001) The Effects of Phyliq (37g/L Laminarin) on Typhlodromus pyri (Acari, Phytoseiidae) on Artificial Substrate in Laboratory: LR 50 Estimation and Reproduction Assessment . Project Number: 01TYGOL24. Unpublished study prepared by Promo-Vert S.A. 22 p.	24-Oct-2007
47283300	Laboratories Goemar SA (2007) Submission of Product Chemistry Data in	15-Nov-

	Support of the Application for Registration of VacciPlant and the Petitions for Tolerance of Laminarin for Use on Food Crops. Transmittal of 2 Studies.	2007
47283301	Trebert, R.; Cousin, C. (2002) Laminarin-Analytical Profile of One Batch 96S51. Project Number: BPL/200111/0388. Unpublished study prepared by Crepin Analyses & Controles. 54 p.	15-Nov-2007
47283302	Comb, A. (2006) Iodus 40: Two Year Storage Stability. Project Number: GOM/005, GOM/005/063905. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 32 p.	15-Nov-2007
47391100	Laboratoires Goemar SA (2008) Submission of Product Chemistry and Toxicity Data in Support of the Application for Registration of VacciPlant and the Petition for Tolerance of Laminarin for Use on Food Crops.	02-Apr-2008
47391101	Smith, F. (2008) Product Identity and Composition, Description of Beginning Materials and Description of Formulation Process: (VacciPlant). Unpublished study prepared by SciReg, Inc. 52 p.	02-Apr-2008
47391102	Smith, F. (2008) Toxicology Waiver Request- Acute Inhalation Toxicity: (VacciPlant). Unpublished study prepared by SciReg, Inc. 65 p.	02-Apr-2008

B. EPA Risk Assessment Memoranda

Rexrode, M. Science Review in Support of New Product Registration Human Tolerance Application for VacciPlant, an End-use Product Containing the Active Ingredient Laminarin (3.5%) dated October 23, 2009.

Rexrode, M. Science Review in Support Support of a Tolerance Exemption Petition, Registration of an End-Use Product for VacciPlant that Contains Laminarin (3.5%) (3.5%) dated October 28, 2008.

C. References

U.S. EPA. 1998. Guidance for Ecological Risk Assessment. Risk Assessment Forum. EPA/630/R-95/002F, April 1998.

U.S.EPA 2008. Terrestrial Residue Exposure Model (T-REX) Version 1.4.1. EFED/OPP/USEPA.

U.S.EPA 2004. Individual Effects Chance Model Version 1.1. EFED/OPP/USEPA.

U.S. EPA. 2004. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs. Office of Prevention, Pesticides, and Toxic Substances. Office of Pesticide Programs. Washington, D.C. January 23, 2004.

APPENDIX A – BIOCHEMICAL PESTICIDE DATA REQUIREMENTS

TABLE 1. Physical/Chemical Properties for Laminarin

TABLE 1.0 Physical and Chemical Properties for pure TGAI Laminarin[a]			
Guideline Reference No.	**Property**	**Description of Result**	**Methods**
830.6302	Color	White	MRID 47264908
830.6303	Physical State	Powder	MRID 47264908
830.6304	Odor	Low odor	MRID 47264908
830.6313	Stability	Stable after 14 days at 54°C in the presence of aluminum acetate or aluminum	MRID 47264909
830.6314	Oxidation/Reduction: Chemical Incompatibility	No oxidizing properties	MRID 47264911
830.6315	Flammability	None flammable; neither development nor ignition of gas were observed after contact with water. An exothermic reaction was observed at 236°C±3°C (mean value). No self-ignition temperature was recorded up to 420°C.	MRID 47264912 MRID 47264913 MRID 47264914
830.6316	Explodability	Not explosive	MRID 47264915, checking heat, friction, and shock sensitivity
830.6317	Storage Stability	Not required for TGAI	
830.6319	Miscibility	Not applicable, product is not an emulsifiable liquid and will not be diluted with petroleum solvents.	
830.6320	Corrosion Characteristics	Not required for TGAI	
830.6321	Dielectric Breakdown Voltage	Not required for TGAI	
830.7000	pH	6.25±0.02 at 23.2°C (1% w/v)	MRID 47264920, by pH meter and a glass electrode
830.7100	Viscosity	Not required for TGAI	

TABLE 1.0 Physical and Chemical Properties for pure TGAI Laminarin[a]			
Guideline Reference No.	**Property**	**Description of Result**	**Methods**
830.7200	Melting Range	No melting point could be determined. The test material became yellow at 204-215C, then it turned brown at 216-225.2C. At about 310.6-316.2C, the test material was completely retracted and blacked colored. The test material probably degraded during the test.	MRID 47264916, by using an Electrothermal 8103 apparatus
830.7220	Boiling Range	The test material is a powder.	
830.7300	Relative Density	D_4^{20} = 1.515±0.04 - 1.502±0.06	MRID 47264917 and 47264918, by pycnometric method
830.7370	Dissociation Constant in Water	Can not be determined.	
830.7550	Partition Coefficient	Log P = -1.6	MRID 47264928, by shake flask method
830.7840	Water Solubility	> 88.6 g/L at 20°C; < 10 mg/L (n-heptane); < 10 mg/L at 20°C (xylene, 1,2-dichloroethane, and ethyl acetate); 60 mg/L (methanol); 21 mg/L at 20°C (acetone)	MRID 47264919 MRID 47264921 MRID 47264922 MRID 47264923 MRID 47264924 MRID 47264925 MRID 47264926 by flask method
830.7950	Vapor Pressure	< 2.6 x 10^{-5} Pa at 25°C	MRID 47264927, using a vapor pressure balance system

TABLE 2. Toxicity Data Requirements Summary

Table 2. 0 Toxicological Results/ Category			
Guideline # Test	**Results/Toxicology Category**	**MRID**	**Study Conclusion**
870.1100 Acute Oral	LD_{50}>2,000 mg/kg III	47264930 47264943	Acceptable
870.1200 Acute Dermal	LD_{50}>5,000 mg/kg IV	47264931 47264974	Acceptable
870.1300 Acute Inhalation	> 1.02 mg/L III	47264932	Acceptable
870.2400 Primary Eye Irritation	Non irritating IV	47264933 47264976	Acceptable
870.2500 Primary Dermal	Non- irritating IV	47264934	Acceptable

Table 2. 0 Toxicological Results/ Category			
Guideline # Test	**Results/Toxicology Category**	**MRID**	**Study Conclusion**
Irritation-Rabbits			
870.2600 Dermal Sensitization	Not a sensitizer IV	47264935 47264978	Acceptable
Acute Subcutaneous	LD_{50}>1,000 mg/kg	47264936	Acceptable
870.3050 28 day Oral Toxicity-Rat	NOEL=1,000 mg/kg/day	47264937	Acceptable
870.3100 90 day Oral Toxicity-Rat	NOEL=1,000 mg/kg/day	47264938	Acceptable
870.3150 Subchronic Oral Toxicity (gavage) - Dog	NOEL=1,000 mg/kg/day	47264939	Acceptable
870.3700a Prenatal Developmental Toxicity Study - Rat	Maternal NOEL $\geq$ 1,000 mg/kg/day Developmental NOEL > 1,000 mg/kg/day	47264940	Acceptable
870.3700b Prenatal Developmental Toxicity Study - Rabbit	Maternal LOAEL = 1,000 mg/kg/day Developmental LOAEL = 1,000 mg/kg/day	47264941	Acceptable
870.5100 Bacterial Reverse Mutation Test	There was no evidence of induced mutant colonies over background	47264942	Acceptable
870.5300 *In Vitro* Mammalian Cells in Culture Gene Mutation Assay	There was no evidence of induced mutant colonies over background.	47264943	Acceptable
870.5395 Bone Marrow Micronucleus assay in mouse	No toxicity was noted in either sex at any dose up to the limit dose of 2000 mg/kg bw	47264944	Acceptable
870.7800 Immunotoxicity	**Waiver Request**	47264945	Acceptable

TABLE 3. EcoToxicity Data Requirements Summary

Table 3.0 Ecotoxicity Data			
Guideline # Test	**Results/Toxicology Category**	**MRID**	**Study Conclusion**
850.1010 Acute Toxicity Test, Daphnids	EC_{50} >100 mg/L.	47264947	Acceptable
850.1075 Acute Toxicity Freshwater Fish *Danio rerio*	96 hr LC_{50} >100 mg/L.	47264948	Acceptable
850.1075	96-hr LC_{50} >100 mg/L.	47264949	Acceptable

Table 3.0 Ecotoxicity Data			
Guideline # Test	**Results/Toxicology Category**	**MRID**	**Study Conclusion**
Fish Acute Freshwater Rainbow Trout *Oncorhynchus mykiss*			
850.2100 Avian Acute Oral Toxicity Bobwhite (*Colinus virginianus*)	LD_{50} >2000 mg/kg	47264950	Acceptable
850.2200 Avian Dietary Toxicity Bobwhite (*Colinus virginianus*)	LC_{50} >5000 ppm	47264951	Acceptable
850.3020 Acute Contact Toxicity Honey bee (*Apis mellifera)*	LD_{50} >118.64 µg/bee 48-hr contact LD_{50} >100.00 µg/bee.	47264952	Acceptable
850.5400 Algal Toxicity, Tiers I and II Green alga *Selenastrum capricornutum*.	E_bC_{50}, E_rC_{50}, NOECb, and NOECr for the test material at 24, 48, and 72 hours were each >100 mg/L	47264953	Acceptable
835.3110 Biodegradability	Biodegradation in the reference material and toxicity controls was 71% and 65%, respectively, after 14 days. Laminarin was concluded to be readily biodegradable under the test conditions.	47264954	Acceptable
880.4350 Nontarget Insect Testing	Exposure to 10.0 L/ha of the test material did significantly lower the fecundity of *A. rhopalosiphi* females compared to the untreated control. However, the product label for Vacciplant recommends an application rate of 9.7 to 14.4 oz/A, which the reviewer calculates to be equivalent to 0.7 to 1.05 L/ha, well below the 10.0 L/ha rate at which fecundity was affected.	47264979	Acceptable