Docket Number EPA-HQ-OPP-2007-0566

Chitin and Chitosan
Final Registration Review Decision
Case 6063

Chitin - PC Code 128991
Chitosan - PC Code 128930

Approved by: _____

Janet L. Andersen, Director
Biopesticide and Pollution Prevention Division

Date: 12/11/08

Approved by: _____

Joan Harrigan-Farrelly, Director
Antimicrobials Division

Date: 12/11/08

Chitin and Chitosan Registration Review Team

Human Health, Environmental Effects, & Risk Management
Russell S. Jones, Ph.D., Senior Biologist, Biochemicals Branch/BPPD
Roger Gardner, Senior Toxicologist, Biochemicals Branch/BPPD

Risk Manager
Chris Pfeifer

Biochemical Pesticides Branch Chief
Linda Hollis

Biopesticides &Pollution Prevention Division Special Assistant
Stephen Morrill

Antimicrobials Division Team Leader
Diane Isbell

Office of General Counsel
Philip Ross

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I. INTRODUCTION

This is EPA's Final Registration Review Decision for Chitin and Chitosan and is being issued pursuant to 40 CFR Sections 155.57 and 155.58. A registration review decision is the Agency's determination whether a pesticide meets, or does not meet, the standard for registration in FIFRA. For additional information on Chitin and Chitosan, additional documents can be found in EPA's public docket (Docket # EPA-HQ-2007-0566) at www.regulations.gov.

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

In 2006, the Agency implemented the new Registration Review program pursuant to FIFRA Section 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

Pursuant to 40 CFR Sec. 155.50, the Agency formally initiated registration review for Chitin and Chitosan with the following timeline:

- September 19, 2007 - Publication of a Preliminary Work Plan (PWP) in the initial docket for Chitin and Chitosan (EPA- HQ-OPP-2007-0566).
- September 19, 2007 to November 19, 2007 – Two comments were received and discussed in the Final Work Plan (FWP). The comments were non-substantial and did not change the work plan or timeline. (Directions for opportunity for further comment can be found below in Section II F.)
- January 8, 2008 - Issuance of a Final Work Plan (FWP) addressing the public comments and stating that the most recent exposure and risk assessments still supported the registration of the currently registered pesticide products containing Chitin and Chitosan and met the requirements of registration review under 40 CFR Sec. 155.50.
- August 6, 2008 - Issuance of a Proposed Registration Review Decision in the docket for public comment. Comment period closed on December 6, 2008. The Agency received one comment regarding pharmaceutical uses of Chitin that did not apply to this decsion.

Data and information evaluated to support Chitin and Chitosan, as published in the PWP, are summarized herein. Additional information will soon be available in the Chitin and Chitosan Biopesticide Registration Action Document (BRAD) located on the biochemical pesticides website *(http://ww.epa.gov/pesticides/biopesticides).*

On October 26, 2007, the Agency issued a Final Rule in the Federal Register (FR) on the data requirements to support registration of biochemical and microbial pesticides, and updated definitions for both biochemical and microbial pesticides (FR Volume 72, Number 207) [Page 60988-61025]. The rule became effective on December 26, 2007. The data and information evaluated for the Preliminary Work Plan (PWP) were considered in light of these requirements. The final rule did not trigger further data requirements for the registered pesticide formulations discussed in the PWP.

The data and information evaluated to support Chitin and Chitosan (Case 6063) as published in the PWP continue to support the registrations containing these active ingredients, except in cases where the formulation of the active ingredient has changed, in which case new data and information may be required. The status of these and other registration review cases is available on *http//www.epa.gov/oppsrrd1/registration review/review/.* Further information will be available in the Chitin and Chitosan Biopesticide Registration Action Document (BRAD) and located on the biochemical pesticides website once it is completed. (*http//www.epa.gov/pesticides/biopesticides*)

There are two active ingredients in this case – Chitin and Chitosan. Chitin is a naturally occurring chain of glucose molecules that is structurally related to cellulose, and is ubiquitous in nature. Its chemical name is Poly-N-Acetyl-D-Glucosamine. Chitin is most commonly derived from crustacean shells, particularly from crabs and shrimp. Historically, it has been used as a food additive and a fertilizer. As a pesticide active ingredient, it acts by stimulating the growth of certain microorganisms in soil, which release substances that kill pathenogenic nematodes and their eggs. The compound is reputed to play a role as a plant growth regulator by bolstering plant defenses against disease.

Chitosan is also a naturally occurring chain of glucose molecules that is structurally related to cellulose. Its chemical name is Poly-D-Glucosamine. It is one of the most common compounds in nature. Commercially, Chitosan is prepared through the deacetylation of Chitin. Chitosan has several biomedical applications. It is considered to be a hemostatic agent that is hypoallergenic and is known to possess anti-bacterial properties. These properties also allow for its use as an active ingredient in anti-microbial pesticides. However, as an agricultural active ingredient, Chitosan is best known as a plant growth regulator that boosts the ability of plants to defend against fungal infections.

Currently, there is one registered product containing Chitin as an active ingredient, and two registered products containing Chitosan as an active ingredient. Chitin is used in this pesticide to control nematodes. It is applied to be incorporated into soil or grass, and has both food and non-food use sites. Of the two Chitosan products, one is used as a plant growth regulator, the other an antimicrobial agent. As a plant growth regulator it is applied through foliar application and aids in defending plants against fungal diseases, mold and mildew. As an antimicrobial, it is primarily used as a fabric treatment to prevent bacterial and fungal growth.

II. SCIENTIFIC ASSESSMENT

A. PRODUCT CHEMISTRY (40 CFR 158.2030)

Chitin: Summary memos, dated March 17, 1988 and January 24, 1990, found acceptable product identity, manufacturing process and a discussion of formation of unintentional ingredients data as well as physical and chemical properties for the TGAI. An ash content analysis submitted in 1992 helped to further clarify the identity of the impurities in the TGAI. Assessments of the product chemistry continue to meet the registration and safety standards as required by FIFRA. Sufficient analytical methodology exists for enforcement and to maintain quality control of the sole Chitin-based pesticide, Clandosan.
Chitosan as a PGR: Product chemistry data (880.1100) were found to be acceptable in EPA's Summary Review Memo for Elexa 4, dated October 11, 2000. Manufacturing process, description of beginning materials, product identity, analytical method, preliminary analysis, batch analysis and verification of certified limits are found in MRIDs 44292301 and 45210703. Assessments of the product chemistry of that original formulation continue to meet the registration and safety standards as required by FIFRA. Sufficient analytical methodology exists for enforcement and to maintain quality control of Elexa 4.

Chitosan as an antimicrobial: Product chemistry submissions for the antimicrobial product Chitosante, found in MRIDs 46248901 and 4588601-4588606, were sufficient to satisfy product chemistry data requirements for an antimicrobial. Chitosante was registered on July 23, 2003.

The product chemistry reviews for Chitin and Chitosan are located in the Chitin registration review docket (EPA-HQ-OPP-2007-0566).

B. HUMAN HEALTH

1. Acute Toxicity (40 CFR Part 158.2050)

Chitin: The registrant submitted studies and waiver requests that satisfy the requirements for toxicity studies for Clandosan. The toxicity data submitted and waiver requests submitted by the registrant are considered sufficient to satisfy the current biochemical toxicity data requirements. Acute oral toxicity and primary eye irritation studies were found acceptable, and were characterized as Toxicity Category IV in an HED Summary Memo dated January 5, 1988. Per the review, data requirements for acute dermal toxicity, acute inhalation toxicity and primary dermal irritation were satisfied through adequate waiver requests; and it was determined that Chitin was not considered to be a dermal sensitizer.
Chitosan as a PGR: The toxicity data submitted by the registrant are considered sufficient to satisfy the current biochemical toxicity data requirements. A Summary Memo from Carol Frazer of BPPD dated January 23, 2001 captures the results of the review. Acute oral toxicity and acute inhalation toxicity are characterized as Toxicity Category IV (MRIDs 44931205 and 45210702 respectively). Acute dermal toxicity, primary eye irritation and primary dermal irritation are all characterized as Toxicity Category III (MRIDs 45210701, 44931206 and 45264301 respectively). Data submitted for the registration of Elexa indicate that Chitosan is not

considered to be a dermal sensitizer (Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002.).
Chitosan as an antimicrobial: A July 1, 2003 Summary Memo from the Antimicrobials Division confirms the acceptability of the toxicity data with regard to current antimicrobial data requirements. Acute oral toxicity, acute dermal toxicity, acute inhalation toxicity, and primary dermal irritation are all characterized as Toxicity Category IV (MRIDs 45886507, 45895201, 45886508 and 45886509 respectively). Primary eye irritation (MRID 45886510) is characterized as Toxicity Category III. Chitosan is not considered to be a dermal sensitizer (MRID45886511).

2. Subchronic Testing (40 CFR Part 158.2050)

Registrants submitted waiver requests and cited public literature to satisfy requirements for both oral and dermal sub-chronic studies for both Chitin and Chitosan.

Chitin: The data requirement for Chitin was satisfied on the basis of the information submitted for Chitosan. The two ingredients are considered sufficiently similar so as to allow the information that was used to satisfy the data requirement for Chitosan to be bridged to Chitin (RD Recommendation Memo dated March 17, 1988).
Chitosan as a PGR: Waivers for subchronic data requirements were accepted in a review associated with a tolerance reassessment for Chitosan (Rita Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002). The rationales for the waivers were founded on the low concentrations of the active ingredient in pesticide products, the ingredient's low toxicity and the natural ubiquity of the ingredient in the environment.
Chitosan as an antimicrobial: Not applicable.

3. Developmental Toxicity (40 CFR Part 158.2050)

Developmental toxicity testing requirements for Chitin and Chitosan were satisfied by waivers in the manner referenced in the Subchronic Testing section above. Again, the rationales for the waivers were founded on the low concentrations of the active ingredient in pesticide products, the ingredient's low toxicity and the natural ubiquity of the ingredient in the environment (Rita Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002).

4. Mutagenicity Testing (40 CFR Part 158.2050)

Mutagenicity testing requirements for Chitin and Chitosan were satisfied in the same manner as the subchronic toxicity data requirements (Rita Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002).

5. Immunotoxicity Testing (40 CFR Part 158.2050)

Immunotoxicity testing requirements for Chitin and Chitosan were satisfied in the same manner as those referenced above. However, any future incidents of hypersensitivity resulting from the labeled uses of Chitin or Chitosan products, reported in accordance of 6(a)(2) of

FIFRA, may result in the requirement of immune response studies (Rita Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002). No incidents of hypersensitivity have been reported as of the time of this review.

6. Chronic Testing/Special Testing (40 CFR Part 158.2050)

Chronic exposure studies are conditionally required to support food uses of biochemical pesticides only if 1) potential adverse effects are indicated, based on the subchronic effect levels based in Tier I subchronic studies, 2) the pesticide use pattern justifies it, or 3) if repeated human exposure is expected. Oncogenicity studies are required to support food uses only if the active ingredients or any of their metabolites, degradation products or impurities produce (in Tier I studies) morphologic effects in any organ that could potentially lead to neoplastic changes. Agency scientists have determined that the triggers for chronic exposure and oncogenicity testing for Chitin and Chitosan have not been met; and at this time the Agency is not requiring those studies (Rita Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002).

7. Effects on the Endocrine System

EPA is required under Section 408(P) of the Federal Food and Drug Administration (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide product active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that it include evaluations of potential effects in wildlife.

The Agency has no knowledge of either Chitin or Chitosan being an endocrine disruptor. Consequently, endocrine-related concerns did not adversely impact the Agency's safety finding for Chitin or Chitosan.

When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been developed and vetted, Chitin and Chitosan may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption (Rita Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002).

8. FQPA Assessment: Dietary Exposure and Risk Characterization

The data requirements required for FQPA risk assessments for Chitin and Chitosan have been satisfied on the basis of the information submitted for Chitosan. The two ingredients are sufficiently similar so as to allow the information that was used to satisfy the data requirement for Chitosan to be bridged to Chitin (RD Recommendation Memo dated March 17, 1988, Rita

Kumar Memo dated August 11, 1997 and Tolerance Reassessment Eligibility Document for Chitosan dated July 3, 2002).

Chitin:

Tolerance: On March 30, 1988, an 'Exemption from The Requirement of a Tolerance' was established for Chitin under 40 CFR 180.1089. The exemption permits the use of Chitin on "a variety of agricultural crops." A tolerance reassessment, completed September 12, 2003, confirmed that the data on file were sufficient to support this use with regard to FQPA considerations.

Dietary Exposure; Acute and Chronic Dietary Risks for Sensitive Subpopulations, Particularly Infants and Children: Dietary exposure to Chitin occurs regularly because this compound is ubiquitous in nature, and incidentally present in many of our foodstuffs. It is, likewise found in many dietary supplements. To date, no risks have been associated with its consumption. Additional dietary exposures to Chitin residues, and the risk posed by ingestion of foods treated with the pesticide, are likely to be minimal for adults, infants and children. With regard to food uses, applications are infrequent and are made directly to the soil, minimizing the opportunity for exposure. In the unlikely event that foodstuffs contained the pesticidal residues of Chitin, no human health risks are expected. The lack of acute oral toxicity/pathogenicity extends to incidental consumption; and data confirm that there is no dietary exposure, aggregate or cumulative, which exceeds the Agency's LOC. Given low application rates, low toxicity and a lack of toxic endpoints, the risks associated with dietary exposure are negligible.

Drinking Water Exposure and Risk Characterization: The Agency has determined that there will be negligible exposure to residues in drinking water resulting from the pesticidal use of Chitin. Applications of Chitin are infrequent; application rates are low; and applications are made directly into the soil or to the ground through saturation. The chances of Chitin being transferred to ground water are negligible. Chitin is biodegradable, and is not known to accumulate in water, except in relation to algal growth. In the unlikely event of exposure, no hazards are expected. Chitin is already used in medicines and the purification of water without reported incident. Furthermore, Chitin is present in insects and many edible plants; and it is incidentally consumed on a regular basis. Given low application rates, low toxicity and a lack of toxic endpoints, the risks associated with drinking water are negligible.

Risks Posed by Potential Non-Occupational Residential, School or Daycare Exposure: Exposures to adults, infants and children via treated lawns or recreational areas are likely if the pesticide is used as labeled. However, potential exposure is minimal because applications are infrequent and application rates are low. Furthermore, the pesticide is naturally occurring and ubiquitous in the environment; and there is no history of hazard related to exposure. Based on the low toxicity potential as evidenced by the data submitted, potential non-occupational risks are negligible.

Aggregate Exposure: The Agency has considered the various routes of exposure (dietary, drinking water, and exposure from non-occupational sources) and potential risks of this biochemical pesticide. The proposed use of the active ingredient does not pose significant risk to populations including infants and children. This decision is based on the low toxicity potential as demonstrated by the information submitted in support of the registration of the end use product Clandosan.

Safety Factor: Based on the low toxicity, lack of toxic endpoints, and the low exposure potential of Chitin, the 10 X safety factor was not required to assess dietary risks to infants and children.

Chitosan as a PGR:

Tolerance: An 'Exemption from The Requirement of a Tolerance' was established in 1986 for Chitosan under 40 CFR 180.1072 for seed treatments. The exemption was amended on April 19, 1995 to include "any raw agricultural crops." A tolerance reassessment was completed on July 3, 2002. It found that the information on file was sufficient to maintain the tolerance relative to FQPA considerations. The review based its approval on the following information: 1) the original literature and data submitted in 1986 characterizing Chitosan's lack of toxicity; 2) approval by the FDA for use of Chitosan as a food additive; 3) an extensive history of human use and exposure, without record of incident; and 4) the relatively low application rates. With regard to the recent standards of the Food Quality Protection Act, a tolerance reassessment involved product specific toxicological data and all applicable biochemical pesticide toxicology data requirements. Studies were submitted and approved for all Tier I biochemical toxicology data requirements. Waiver requests were made and accepted for all other toxicological data requirements. Accordingly, the Agency does not anticipate that a human health risk assessment will be needed for Chitosan when it is used as a PGR or as a fungicide used on plants.

Dietary Exposure; Acute and Chronic Dietary Risks for Sensitive Subpopulations, Particularly Infants and Children: Dietary exposure to Chitosan occurs regularly because this compound is ubiquitous in nature, and incidentally present in many of our foodstuffs. It is also an oft-consumed dietary supplement. To date, no risks have been associated with its consumption. Additional dietary exposures to Chitosan residues, and the risk posed by ingestion of foods treated with the pesticide, are likely to be minimal for adults, infants and children by the oral route: the concentration of Chitosan in the pesticide is low; applications are well-diluted; and chitosan biodegrades quickly. Data submitted with the registration of the end use product show that the pesticidal residues associated with the agricultural use of Chitosan can be orders of magnitude less than what occurs in a verdant environment. In the unlikely event that foodstuffs contained the pesticidal residues of Chitosan, no human health risks are expected. The lack of acute oral toxicity extends to incidental consumption; and data confirm that there is no dietary exposure, aggregate or cumulative, which exceeds the Agency's LOC. Given low application rates, low toxicity and a lack of toxic endpoints, the risks associated with dietary exposure are negligible.

Drinking Water Exposure and Risk Characterization: The Agency has determined that there will be negligible exposure to residues in drinking water resulting from the pesticidal use of Chitosan. Application rates are low; applications are dilute; and Chitosan readily biodegrades in water. The chances of Chitosan being transferred to ground water are also negligible for these reasons. In the unlikely event of exposure to Chitosan in drinking water, no hazards are expected. Chitosan is already used in medicines and the purification of water without reported incident. Given low application rates, low toxicity and a lack of toxic endpoints, the risks associated with Chitosan residues in drinking water are negligible.

Risks Posed by Potential Non-Occupational Residential, School or Daycare Exposure: Exposures to adults, infants and children via treated lawns or recreational areas are likely if the pesticide is used as labeled. However, potential exposure is minimal because applications are

dilute, and Chitosan readily biodegrades. Furthermore, the pesticide is a naturally occurring and ubiquitous in the environment; and there is no history of hazard related to exposure. Based on the low toxicity potential as evidenced by the data submitted, potential non-occupational risks are negligible.

Aggregate Exposure: The Agency has considered the various routes of exposure (dietary, drinking water, and exposure from non-occupational sources) and potential risks of this biochemical pesticide. The proposed use of the active ingredient Chitosan does not pose significant risk to populations including infants and children. This decision is based on the low toxicity/pathogenicity potential as demonstrated by the information submitted in support of the registration of the end use product Elexa 4.

Safety Factor: Based on the low toxicity, lack of toxic endpoints, and the low exposure potential of Chitin, the 10 X safety factor was not required to assess the dietary risks to infants or children.

Chitosan as an Antimicrobial: There is no dietary exposure with this use pattern. As such, 'Dietary Exposure and Risk Characterization' are not applicable.

9. Occupational Exposure and Risk Characterization (40 CFR Part 158.2050)

The Agency conducted an occupational assessment for all end use products containing Chitin and Chitosan. The risks to applicators, mixers/loaders and other handlers are expected to be negligible. Given the methods of application, the low concentrations applied, and the infrequency of applications, exposures are expected to be minimal in the case of all end use products. In the case of Chitin, data actually indicate that agricultural residues were often an order of magnitude less than that found in the environment. Nonetheless, personal protective equipment has been required on the labels to mitigate potential occupational exposures as befits the products' respective use profiles. Given the low toxicity profile, Chitin and Chitosan's ubiquity in nature without reported toxicological incident, and the existing label requirements for personal protective equipment, occupational risks are considered negligible.

10. Human Health Risk Characterization

The human hazard assessments and exposure assessments for Chitin and Chitosan indicate that the risks to human health are negligible to non-existent when products containing Chitin and Chitosan are used in accordance with the label. These assessments are considered complete and current, and satisfy the standards of registration review.

All biochemical pesticide toxicology data requirements applicable to a human health effects determination for Chitin were considered and fulfilled for the Chitin-based pesticide CLANDOSAN 618 in 1988. Acute Oral Toxicity and Acute Eye Irritation studies specific to the pesticide were both accepted as Toxicity Category IV. The balance of the Tier I biochemical toxicology data requirements were satisfied through a public literature submission, which further supported the case for Chitin's low toxicity profile. Additional information used in making a human health effects determination for Chitin included: 1) a bridging of data used to establish an exemption from the requirement of a tolerance for Chitosan; 2) an approval by the FDA for the

use of Chitin as a food additive; 3) a history of unrestricted use of Chitin as a soil amendment, without a record of incident; and 4) a recognition that any exposure gains relative to pesticidal applications would be negligible, given Chitin's ubiquity in nature. Altogether, the aforementioned information provided sufficient grounds for section 3 registration and an exemption from the requirement of a tolerance for Chitin – 40 CFR 180.1089. As a result of these considerations, the Agency finds the human health risk assessment for Chitin sufficient to satisfy the standards of registration review.

Human health effects were considered with regard to each use pattern of Chitosan. As a PGR and fungicide applied to plants, the Agency finds that no additional human health effects data will be required for Chitosan, provided the source of the active remains unchanged. Reviews indicate that data were sufficient to fulfill all current biochemical pesticide toxicology data requirements for Chitosan. Reviews considered the following information: 1) the original literature and data submitted in 1986 characterizing Chitosan's lack of toxicity; 2) approval by the FDA for use of Chitosan as a food additive; 3) an extensive history of human use and exposure, without record of incident; and 4) the relatively low application rates. With regard to the standards of the Food Quality Protection Act, a tolerance reassessment involved product specific toxicological data and all applicable biochemical pesticide toxicology data requirements. Studies were submitted and approved for all Tier I biochemical toxicology data requirements. Waiver requests were made and accepted for all other toxicological data requirements. The Agency completed tolerance reassessment for Chitosan on July 3, 2002. Accordingly, the Agency finds the human health risk assessment for Chitosan (per the source of the active ingredient reviewed in the PWP) sufficient to satisfy the standards of registration review.

With regard to Chitosan's use as an antimicrobial agent, the Agency has considered all applicable toxicology data requirements. A July 2003 summary memo notes the following toxicological profile for the sole end-use product, Chitosante: Acute Dermal Toxicity, Acute Oral Toxicity, Acute Inhalation Toxicity and Skin Irritiation are accepted as Toxicity Category IV; Acute Eye is accepted as Toxicity Category III; and Chitosante is deemed a non-sensitizer. Based on the toxicity profile of the end-use product and reviews characterizing the health effects of Chitosan, the Agency finds the human health risk assessment for Chitosan, when used as an antimicrobial, sufficient to satisfy the standards of registration review.

Human health hazard and exposure scientific reviews are located in the Chitin and Chitosan registration review docket (EPA-HQ-OPP-2007-0566).

C. ECOLOGICAL EFFECTS

Ecological effects for Chitin were fully considered in the course of reviewing the application for the first product containing this active ingredient (CLANDOSAN 618). A registration decision document, issued in March of 1988, concluded that Chitin posed negligible to non-existent ecological risk. In that decision document, the Agency granted data waivers for all nontarget data requirements relating to the application of the Chitin-based pesticide, CLANDOSAN 618. It was determined that under normal conditions, the proposed end uses would pose minimal hazards to nontarget organisms. EPA noted the following as grounds for a

rationale: 1) historical data on Chitin demonstrating negligible toxicity on humans and animals; 2) a ubiquity of Chitin in nature such that applications of Chitin would likely fall within the existing range of background concentrations; and 3) the ability of Chitin to degrade. As a result of these considerations and an 'Agency Nontarget Effects and ESA Assessment,' done on April 7, 2008, the Agency finds the ecological risk assessment for Chitin sufficient to satisfy the standards of registration review.

With regard to Chitosan's initial use as a PGR, ecological effects were first considered in 1986 when the applicant Natural AG submitted a mix of general animal toxicity data and waiver requests to fulfill their nontarget data requirements in support of EPA Reg. No. 56437-1. Subsequent registrations for Hyga, ELEXA, and ELEXA-4 were all granted waivers for their nontarget requirements based on like rationales. The most recent review of nontarget waiver requests occurred for ELEXA-4 in March of 2000. The review took place in the Biopesticides and Pollution Prevention Division (BPPD) and reflects the most current thinking on ecological effects relative to Chitosan. In that review, it was determined that under normal conditions, the proposed end uses would pose minimal hazards to nontarget organisms. BPPD noted the following as grounds for its waivers: 1) copious amounts of historical data on Chitosan demonstrating negligible toxicity on humans and animals; 2) a ubiquity of Chitosan in nature such that proposed application rates would likely fall within the existing range of background concentrations; and 3) the ability of Chitosan to decompose. As a result of these considerations, the Agency finds the ecological risk assessment for Chitosan (per the source of the active ingredient reviewed in the PWP), when used as a PGR and fungicide, sufficient to satisfy the standards of registration review.

With regard to Chitosan's use as an antimicrobial agent, the Agency has found that ecological risk is unlikely, and that the information on file is sufficient to support this use pattern vis-à-vis ecological effects. An August 2007 memo from the Risk Assessment and Science Support Branch of the Antimicrobials Division makes the following points in support of this position: 1) Most uses are indoors and allow for minimal environmental exposure. 2) Chitosan is a naturally occurring compound that is common in nature; and no adverse ecological effects have thus far been attributed to its presence. 3) Available information and the prevalent use of Chitosan in food and drugs support the case for Chitosan's relative nontoxicity for mammals. In summary, the Agency finds the ecological risk assessment for Chitosan, when it is used as an antimicrobial active ingredient on fabrics, sufficient to satisfy the standards of registration review.

1. Avian Testing (40 CFR Part 158.2060)

While waivers were granted for nontarget bird data requirements for all the registrations containing Chitin or Chitosan, as detailed above, the Agency ESA Assessment provides substantiating information with regard to the negligible risks to birds. It notes: "Chitin is present in the exoskeletons of arthropods and, therefore, is a regular component of the diets of insectivorous birds. Chitin and Chitosan have been shown to be relatively indigestible by some birds (Akaki and Duke, 1999; and Razdan and Pettersson, 1994). However, many birds (starlings, raptors, and many seabirds) possess chitinases that aid in the digestion of Chitin,

which serves as a source of protein (MacDonald, 2006). No mortalities have ever been observed in birds fed with diets supplemented with Chitin and Chitosan. No adverse effects are expected to birds when Chitin and Chitosan-containing products are applied in accordance with approved labeling."

2. Aquatic Organism Testing (40 CFR Part 158.2060)

While waivers were granted for nontarget aquatic organism data requirements for all the registrations containing Chitin or Chitosan, as detailed above, the Agency ESA Assessment provides substantiating information with regard to negligible risks to aquatic organisms. It notes: "Chitin is ubiquitous in nature and is a major component of the exoskeletons of aquatic arthropods (insects, crustaceans), the radula of molluscs, and the beaks of cephalpods (squid, octopus), the cell walls of fungi (Campbell, 1996), and the scales of fish (Uawonggul et al. 2002). Chitin is a normal component in the diets of fish (e.g. in the exoskeletons of aquatic arthropods and in the scales of prey fish) and fish possess chitinases that metabolize these dietary Chitins (Matsumiya et al. 2006). No mortalities have been observed in fish fed with diets supplemented with chitin and chitosan. No adverse effects are expected to nontarget aquatic organisms when Chitin and Chitosan-containing products are applied in accordance with approved labeling."

3. Nontarget Plant, Insect, Environmental Fate, Aquatic Fauna Chronis/Lifecycle/Field, and Terrestrial Wildlife Testing (40 CFR Part 158.2060)

While waivers were granted for nontarget plant and insect data requirements for all the registrations containing Chitin or Chitosan, as detailed above, the Agency ESA Assessment provides substantiating information with regard to the negligible risks to nontarget plants and insects. It notes: "Chitin is ubiquitous in nature and is a major component of the exoskeletons of aquatic arthropods (insects, crustaceans). Chitin and Chitosan are intended for use as plant defense "boosters" to protect plants from fungal pathogens via the induction of Systemic Acquired Response (SAR). SAR is a mechanism that stimulates the internal defense mechanisms of plants to resist pathogen infection. In plants, Chitin stimulates the production of chitinases, which are used to degrade the Chitin-containing cell walls of pathogenic fungi (Kramer and Muthukrishnan, 1998). There is no direct activity of Chitin or Chitosan against the pathogen. No adverse effects to nontarget insects and plants are anticipated."

4. Endangered Species Assessment (ESA)

Chitin and its closely related derivative, Chitosan, are not expected to cause any adverse effects in any nontarget organisms, including threatened and endangered species. A **No Effects (NE)** determination was made for both Chitin and Chitosan in an April 7, 2008 Endangered Species Act Assessment. It notes that Chitin, and by extension Chitosan, are ubiquitous in nature and are found in many terrestrial and aquatic species. Chitin and its derivatives are functionally identical and have a non-toxic mode of action. There is no direct activity of the active ingredients against the target pest. Based on the existing data, the Agency has determined that there will be **NO EFFECTS (NE)** of Chitin and Chitosan on threatened or endangered terrestrial

or aquatic species listed by the US Fish and Wildlife Service (USFWS) when products containing Chitin or Chitosan are used in accordance with approved labeling.

5. Ecological Risk Characterization

Based on the reviews of the above stated nontarget organisms and environmental fate studies, and the Endangered Species Assessment, EPA has determined that anticipated risk is not likely to result in unreasonable risk to nontarget organisms or the environment when products containing Chitin or Chitosan are used in accordance with approved label use directions.

Ecological scientific reviews and Endangered Species Assessment is located in the Chitin and Chitosan registration review docket (EPA-HQ-OPP-2007-0566).

D. PRODUCT PERFORMANCE (EFFICACY) (40 CFR Part 158.2070)

Product performance data must be developed for all pesticides. However, the Agency typically does not require applicants to submit such efficacy data unless the pesticide product bears a claim to control public health pests. Since no Chitin or Chitosan product has made a claim against a public health pest, no efficacy data has been requested.

E. INCIDENTS

The National Pesticides Information Center (NPIC) database indicates that there have been no reports of human and domestic animal incidents for products containing Chitin or Chitosan. The Agency will continue to monitor for any incidents related to Chitin or Chitosan.

F. PUBLIC COMMENTS

Pursuant to 40 CFR Sec. 155.50, the Agency formally initiated registration review for Chitin and Chitosan on September 19, 2007 with the opening of a docket and the issuance of a PWP for public comment. The Chitin and Chitosan registration review docket was open for a 90-day comment period beginning September 19, 2007. Two comments were received and discussed in the Final Work Plan found in Docket# EPA-HQ-2007-0566. The comments did not change the work plan or timeline.

G. TRADE IRRITANTS

Through the registration review process, the Agency solicited information on trade irritants and, to the extent feasible, took steps toward facilitating irritant resolution. Growers and other stakeholders were asked to comment on any trade irritant issues resulting from lack of Maximum Residue Levels (MRLs) or disparities in key export markets, providing as much specificity as possible regarding the nature of the concern. Chitin or Chitosan is registered for use as a plant growth regulator and fungicide. In addition, Chitin or Chitosan is registered to treat fabric to prevent bacterial and fungal growth. There are no MRLs established for Chitin or Chitosan. In the course of registration review, the Agency has not received any comments

regarding the existence of any trade irritant issues associated with Chitin or Chitosan. However, the Agency will continue to consider any additional information that might prompt an irritant resolution.

H. WATER QUALITY

Chitin and Chitosan are not identified as a cause of impairment for any water bodies listed as impaired under Section 303(d) of the Clean Water Act, based on information provided at: http://oaspub.epa.gov/tmdl/waters_list.impairments?p_impid=3. No comments regarding water quality and Chitin and Chitosan were received during registration review. Nonetheless, the Agency will continue to consider any additional information submitted with regard to water quality which might suggest the need for new data and/or a new risk assessment.

I. 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. At this time, EPA does not believe that use of the registered pesticide products containing Chitin and Chitosan will cause harm or a disproportionate impact on at-risk communities.

To help address potential environmental justice issues, the Agency sought 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 registered pesticides containing Chitin or Chitosan, compared to the general population. No environmental justice issues were identified for Chitin and Chitosan. For additional information regarding environmental justice issues, visit EPA's website at: *http://www.epa.gov/compliance/environmentaljustice/index.html*.

III. FINAL REGISTRATION REVIEW DECISION

The Agency has determined that no additional data are required at this time to support registrations containing Chitin or Chitosan. Further, EPA proposes that no additional risk mitigation measures or labeling changes are required. The Agency has considered Chitin and Chitosan in light of the standard for registration and safety factors in FIFRA and FFDCA as amended by FQPA. EPA has found that there are not likely to be any unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, or to nontarget organisms or the environment, when currently required label instructions are followed. The Agency has found that it is not necessary to conduct a new risk assessment for this case and is, therefore, issuing a proposed final decision pursuant to 40 CFR 155.58 (c).

As per 40 CFR Sections 155.57 and 155.58, the Agency proposes that the standards for Registration Review have been met and that the registration of the three end use products containing Chitin or Chitosan should be maintained.