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# Chitin and Chitosan Summary Document
# Registration Review: Initial Docket
# September 2007

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## I. PRELIMINARY WORK PLAN

### Introduction:

The Food Quality Protection Act 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. 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/.

The Agency has begun to implement the new Registration Review program pursuant to FIFRA Section 3(g) and intends to review each registered pesticide approximately every 15 years to determine whether it continues to meet the FIFRA standard for registration. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state clearly what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. Chitin and Chitosan are among the first biochemical pesticides to undergo the registration review process and to be reassessed using the most current standards of risk assessment.

Because Chitosan is derived from Chitin, and because both compounds share basic physical characteristics, they have been combined into a single case - Registration Review Case 6063. As a matter of general similarity, Chitin and Chitosan are both naturally occurring polymers that are ubiquitous throughout nature. Structurally, they are related to cellulose and each consists of long chains of glucose molecules. Relationally, Chitosan is a deacetylated product of Chitin, whose chains of glucose are slightly modified. As biochemical active ingredients, they are applied in different use patterns; however, they both demonstrate a low toxicity profile, and are both known for their role in bolstering plant resistance. Based on these factors and the data submitted, no adverse human health or ecological risks are expected as a result of exposure to these compounds, if they are used as labeled. However, if additional information is submitted that warrants further risk assessments, the Agency will then conduct any necessary risk assessment(s). Further information regarding use sites, summaries of health, ecological effects data reviews and endangered species assessments, as well as a list of registered pesticide products containing these active ingredients, is found in Parts II and III in this document.

**Anticipated Risk Assessment and Data Needs:**

***Ecological Risk Assessment:*** Ecological effects for both Chitin and Chitosan were duly considered in the course of reviewing the applications for the first products containing these active ingredients. In each case, non-target data and/or various non-target waiver requests were sufficient to determine that the proposed uses of the pesticides containing these active ingredients posed negligible to non-existent ecological risk. These determinations were captured in both summary science memos and regulatory decision documents. EPA's ecological risk assessments are undergirded by the understanding that both Chitin and Chitosan are naturally occurring, ubiquitous, and regarded as essentially non-toxic to animals. Additionally noteworthy, applications of pesticides containing Chitin or Chitosan are not expected to result in concentrations of the compounds measurably greater than common background concentrations. Accordingly, the Agency anticipates that no additional ecological effects or environmental data are required for either Chitin or Chitosan.

*Endangered Species Act:* Endangered species assessments for Chitin and Chitosan are expected to be completed in October of 2007. The assessment documents will be added to the docket at that time. Potential commenters will also have full opportunity to make comments during the 60 day comment period when the assessment documents are posted in the docket for the *Proposed Registration Review Decision for Chitin* .

***Human Health:*** Based on reviews of human health exposure and summary risk assessments that were conducted when the first pesticides containing these active ingredients were originally registered, the Agency anticipates that no additional human health effects data will be required for either Chitin or Chitosan. The reviews indicate that data were sufficient to fulfill all current biochemical pesticide toxicology data requirements for both Chitin and Chitosan. Moreover, all the data reviewed by the Agency indicate that both Chitin and Chitosan are so low in toxicity as to be considered virtually non-toxic to humans or animals. In further support of Chitin's and Chitosan's lack of toxicity, it is also noted that both ingredients are regularly present in many foods; and both have an exemption from the requirement of a tolerance – 40 CFR 180.1089 and 40 CFR 180.1072, respectively. In sum, the Agency anticipates that no new data or human health risk assessments will be necessary for either Chitin or Chitosan.

**Incidents:**

The OPP Incident Data System (IDS) indicates that there have been no reports of human and domestic animal incidents for products containing either Chitin or Chitosan. The Agency will consider any additional incidents data or comments submitted in response to this docket.

**Efficacy and Label Claims**

The Agency requires and reviews efficacy data for products making labeling claims to control public health pests. A review of the pesticide product labels containing Chitin and Chitosan

reveals no claims against public health pests. Accordingly, no efficacy data will likely be required. Notwithstanding, a full review of label claims remains incomplete pending the final registration review decision. As appropriate, registrants will be required to resolve any outstanding efficacy/labeling concerns in response to that final decision.

**Timeline:**

EPA has created the following estimated timeline for the completion of the Chitin and Chitosan Registration Review case. This schedule is subject to revision should there be a need for a Data Call-in during the registration review process or should other issues arise.

| **Activities** | **Estimated Month/Year** |
|---|---|
| Open Public Comment Period for Chitin and Chitosan Docket | September 2007 |
| Close Public Comment Period | November 2007 |
| Develop Final Work Plan (FWP) | January 2008 |
| Open Public Comment Period for Proposed Reg. Review Decision | FY 2008 3rd Quarter |
| Close Public Comment Period | FY 2008 3rd Quarter |
| Final Decision | FY 2008 4th Quarter |
| Total (years) | 1 |

**Guidance for Commenters:**

The public is invited to comment on EPA's preliminary registration review work plan. Stakeholders are specifically asked to provide any additional information regarding use information and any incident data not already reported to the agency. In addition, the Agency welcomes any comments regarding EPA's risk assessments and its anticipated decision not to conduct further risk assessments. The Agency will carefully consider all comments as well as any additional information or data provided prior to issuing a final work plan for the Chitin and Chitosan case.

Water quality concerns for Chitin and Chitosan are expected to be non-existent since these pesticides are ubiquitous in nature and have a very low toxicity profile. Public comment is invited on any water quality concerns. Similarly, trade irritants aren't expected for this pesticide since it is exempted from the requirements for a tolerance in the U.S. Growers and other stakeholders are asked to comment on any trade irritant issues for this pesticide.

**Next Steps:**

After the comment period closes, the Agency will prepare a Final Work Plan for this pesticide.

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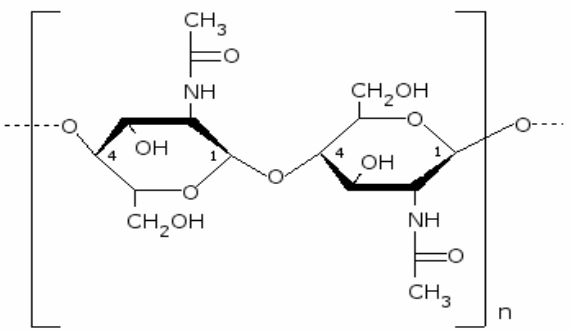
## II. CHITIN FACT SHEET

**Chitin Background Information**:

- Registration review case number: 6063
- Chemical Name: Poly-N-Acetyl-D-Glucosamine
- PC Code: 128991
- CAS#: 1398-61-4
- Source material: Shells of crustaceans
- Sole (and original) registrant: Igene Biotechnology
- First approved for use in a registered product in 1988
- Not subject to reregistration (no Reregistration Eligibility Decision [RED])
- Exemption from The Requirement of a Tolerance: 40 CFR 180.1089; was reassessed September 12, 2003.
- Registration Review Lead: Chris Pfeifer; pfeifer.chris@epa.gov

**Description of the Active Ingredient:**

Chitin is a naturally occurring chain of glucose molecules that is structurally related to cellulose. It is ubiquitous in nature. 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 also reputed to play a role as a plant growth regulator by bolstering plant defenses against disease.




**Chitin**

**Chitin Use Information:**

- Chitin is used for controlling soil nematodes on crops (food and non-food), ornamentals and turf.
- Use sites are residential and commercial. They include: agricultural fields, nurseries, greenhouses, sod farms, commercial turf grasses, golf courses, home lawns and gardens.

- Application methods include: pre-plant soil incorporation and post-plant surface application followed by saturation.
- Mode of action: Chitin acts in soil to stimulate the growth of naturally occurring microorganisms in the soil, which then release substances that kill pathogenic nematodes and their eggs.
- Chitin is the active ingredient in CLANDOSAN 618, which is the sole registered pesticide product containing this active ingredient.

**Recent Actions:**

There have been no recent significant regulatory activities regarding the sole registered Chitin product (i.e. tolerance related actions, changes of use patterns, submission of toxicology studies or incident reports).

**Ecological Risk Assessment Status**:

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, concurred 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, the Agency does not anticipate the need for new data or the need to conduct a new ecological risk assessment for Chitin.

*Endangered Species Act:* An endangered species assessment for Chitin is expected to be completed in October of 2007. The assessment document will be added to the docket at that time. Potential commenters will also have full opportunity to make comments during the 60 day comment period when the assessment document is posted in the docket for the *Proposed Registration Review Decision for Chitin* (FY 2008, 3rd Quarter).

**Human Health Risk Assessment Status:**

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 does not anticipate the need for new data or the need to conduct a human health risk assessment for Chitin.

**Incidents:**

The OPP Incident Data System (IDS) indicates that there have been no reports of human and domestic animal incidents for products containing Chitin. The Agency will consider any additional incidents data or comments submitted in response to this docket.

**Labels and Products:**

The sole registered product with Chitin as an active ingredient follows:
CLANDOSAN 618 (25% a.i.) EPA Reg. No. 54137-1 (formerly EPA Reg. No. 58200-9)

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

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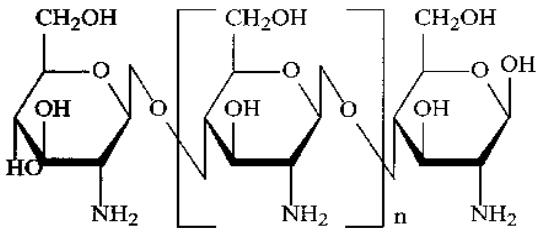
## III. CHITOSAN FACT SHEET

**Chitosan Background Information**:

- Registration review case number: 6063
- Chemical Name: Poly-D-Glucosomine
- PC Code: 128930
- CAS#: 9012-76-4
- Source material: Chitin derived from the shells of crustaceans
- End-use product registrants: Plant Defense Boosters, Inc; Chem-tex, Laboratories, Inc.
- Chitosan was first approved for use as a Plant Growth Regulator (PGR) in a registered product in 1986.
- Chitosan was registered for use as an antimicrobial agent in a registered product in 2003.
- Not subject to reregistration (no Reregistration Eligibility Decision [RED])
- Exemption from The Requirement of a Tolerance: 40 CFR 180.1072; was reassessed July 3, 2002.
- Registration Review Lead: Chris Pfeifer; pfeifer.chris@epa.gov

**Description of the Active Ingredients:**

Chitosan is a naturally occurring chain of glucose molecules that is structurally related to cellulose. 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 a pesticidal active ingredient, Chitosan is best known as a plant growth regulator that boosts the ability of plants to defend against fungal infections.




Chitosan

* This diagram of the chemical structure of Chitosan is presented for illustrative purposes, and is intended primarily as a generalized point of comparison with Chitin. The actual chemical structure of Chitosan is subject to substantial variations based on the degree of deacetylation of Chitin.

**Chitosan Use Information:**

- As a pesticide, Chitosan is used as a Plant Growth Regulator (PGR), fungicide and an antimicrobial agent.
- As a PGR, Chitosan's mode of action is characterized by its ability to bolster plant resistance against fungal diseases. Specifically, it purports protection against downy mildew, powdery mildew, early blight, late blight, gray mold, leaf spot, anthracnose and blast.
- PGR use sites include: agricultural fields, nurseries, greenhouses, commercial turf grasses, and home gardens (food and ornamental).
- As a PGR, it is produced in aqueous form and is applied by spray to plants throughout the growing season, with applications every one to two weeks as needed.
- Chitosan is the active ingredient in ELEXA-4, which is the sole registered PGR product containing this active ingredient.
- As an antimicrobial pesticide, Chitosan employs anti-bacterial properties to protect fabrics from bacterial and fungal growth.
- The antimicrobial pesticide is produced as an aqueous solution and is either applied by spray or added to laundry's wash cycle.
- Chitosan is the active ingredient in ChitoSante, which is the sole antimicrobial pesticide containing this active ingredient.

**Recent Actions:**

There have been no recent significant regulatory activities regarding either Chitosan product, (i.e. tolerance related actions, changes of use patterns, submission of toxicology studies or incident reports).

**Ecological Risk Assessment Status**:

As an active ingredient, Chitosan is employed in three distinct use patterns – as a PGR, as a fungicide on plants, and as an antimicrobial agent. Ecological effects were considered with regard to each use pattern.

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 non-target data requirements in support of EPA Reg. No. 56437-1. Subsequent registrations for Hyga, ELEXA, and ELEXA-4 were all granted waivers for their non-target requirements based on like rationales. The most recent review of non-target 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 non-target 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 does not anticipate the need to conduct an ecological risk assessment for the use of Chitosan as a PGR, nor as a fungicide used on plants.

With regard to Chitosan's use as an antimicrobial agent, the Agency has also found that ecological risk is unlikely. An August 2007 memo from the Risk Assessment and Science Support Branch of the Antimicrobials Division notes the following in support of this position: 1) Most uses are indoors and allow for minimal environmental exposure. 2) Available information and the prevalent use of Chitosan in food and drugs support the case for Chitosan's relative nontoxicity. 3) Chitosan is a naturally occurring compound that is common in nature. In sum, the Agency anticipates that no ecological risk assessment will be necessary for Chitosan when it is used as an antimicrobial active ingredient on fabrics.

*Endangered Species Act:* An endangered species assessment for Chitosan is expected to be completed in October of 2007. The assessment document will be added to the docket at that time. Potential commenters will also have full opportunity to make comments during the 60 day comment period when the assessment document is posted in the docket for the *Proposed Registration Review Decision for Chitin* (FY 2008, 3rd Quarter).

**Human Health Risk Assessment Status:**

Human health effects were considered with regard to each use pattern of Chitosan. As a PGR and fungicide applied to plants, the Agency anticipates that no additional human health effects data will be required for Chitosan. Summary reviews indicate that data were sufficient to fulfill all current biochemical pesticide toxicology data requirements for Chitosan. Health effects data for Chitosan were first found sufficient for the registration of EPA Reg. No. 56437-1 and the issuance of an associated exemption from the requirement of tolerance in 1986. The exemption, found under 40 CFR 180.1072, was reaffirmed once more in a 1995 review. 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. The Agency completed tolerance reassessment for Chitosan on July 3, 2002. 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.

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 summary reviews characterizing the health effects of Chitosan, the Agency anticipates that no human health risk assessment will be necessary when Chitosan is used on fabrics as an antimicrobial active ingredient.

**Incidents:**

The National Pesticides Information Center (NPIC) database indicates that there have been no reports of human and domestic animal incidents for products containing Chitosan. The Agency will consider any additional incidents data or comments submitted in response to this docket.

**Labels and Products:**

The following products have Chitosan as an active ingredient:

| | |
|---|---|
| ELEXA-4 (4% a.i.) | EPA Reg. No. 81045-2 |
| ChitoSante (6% a.i.) | EPA Reg. No. 81446-1 |

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.