Trichoderma Species Summary Document: Registration Review

April 2007

Trichoderma species Summary Document
Registration Review: Initial Docket
April 2007

TABLE OF CONTENTS

Part		Page
I.	Preliminary Work Plan (PWP)	3
II.	FACT SHEET – *Trichoderma harzianum* KRL-AG2	7
	Human Health Effects	8
	Ecological Risk Assessment	9
III.	FACT SHEET - *Trichoderma polysporum* and *Trichoderma viride*	10
	Human Health Effects	10
	Ecological Risk Assessment	11
IV.	List of Products	13
V.	Supplementary Information about *Trichoderma harzianum* KRL-AG2 (called T-22)	14
VI	Website addresses	23

Part I. Preliminary Work Plan

Introduction

The Food Quality Protection Act (FQPA) of 1996 mandated a new program: registration review. 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 continue to 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. *Trichoderma spp*. **(case 6050)** is the first microbial pesticide case undergoing registration review with **four** active ingredients registered by **three** separate registrants. The active ingredients in this case are:

- *Trichoderma harzianum* strain T-39 (called T-39) – prior registrant Makhteshim Agan of North America or MANA;
- *Trichoderma harzianum* strain KRL-AG2 ATCC 20847 (called T-22) – registrant BioWorks, Inc.
- *Trichoderma polysporum* ATCC 20475 (called T-75) and *Trichoderma viride* ATCC 20476 (called T-76) – registrant BINAB™ USA, Inc.

These microbial active ingredients occur ubiquitously in the environment. They demonstrate a low toxicity profile, and potential exposure is limited by the types of soil applications and approved label rates and sites. Based on these factors and the data submitted, no adverse ecological risks are expected as a result of exposure to these microorganisms, 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, III** and **V** in this document. The Agency places pesticides in Toxicity Categories I through IV based on data evaluations, review of public literature, and the nature of the inert ingredients. Pesticides placed in Toxicity

Category I pose the greatest toxicological risk and IV the least. Further information about Toxicity Categories can be obtained from 40 CFR 156.62 and 156.64 and EPA's Label Review Manual (see *http://www.epa.gov/oppfead1/labeling/lrm/chap-07.htm).* Another source of information about biopesticides is the Biopesticides and Pollution Prevention (BPPD) website *(http://www.epa.gov/pesticides/biopesticides).*

Anticipated Risk Assessment and Data Needs

Health

Trichoderma harzianum T-39

This active ingredient was conditionally registered by MANA in May 2000 and voluntarily canceled at the registrant's request by non-payment of maintenance fees (70 FR 44637; July 21, 2005). The exemption from tolerance for residues of *Trichoderma harzianum* T-39 on all food commodities met the FQPA1996 safety standard (40 CFR 180.1201, 65 FR 38753; June 22, 2000). However, there is no registrant for this active ingredient at this time. The Agency will take separate action to propose revocation of this exemption from tolerance.

Trichoderma harzianum T-22

Based on previously completed reviews of human health exposure and summary risk assessments, the Agency anticipates that no additional health effects data are required for the currently registered sites for *Trichoderma harzianum* T-22. Reviews of toxicity/pathogenicity studies, of public literature, and of scientifically based data waiver requests, place this pesticide in Toxicity Category III and IV which pose minimal risk to health and the environment when the pesticides are used as labeled. For additional information, refer to the **Fact Sheet** and **Supplementary Information** for T-22 in **Parts II and V** in this document.

An initial exemption from tolerance for residues of T-22 was established for seed treatments on certain commodities (40 CFR 180.1102, 55 FR 50327; December 6, 1990). This tolerance exemption was later revised and reassessed to include all food/feed commodities (40CFR 180.1102, 64 FR 16856, April 7, 1999; 55 FR 37375; June 14, 2000), and found to meet the FQPA 1996 safety standard (see BBPD website *http://www.epa.gov/pesticides/biopesticides* for Federal Register Notice). The Agency has not identified any dietary, aggregate or cumulative risk that exceeds the Agency's Level of Concern (LOC) for T-22.

Trichoderma polysporum T-75, *and Trichoderma viride* T-76

Based on previously completed reviews of human health exposure and summary risk assessments, the Agency anticipates that no additional health effects data are required for the currently registered sites for *Trichoderma polysporum* and *Trichoderma viride* T-75 and T-76. These strains are not registered for food uses. For additional information, refer to the **Fact Sheet** included for T-75 and T-76 in **Part III** this document.

Ecological Effects

Based on use patterns, low exposure levels, and low toxicity potential, no additional ecological effects or environmental data are required for the currently labeled pesticide products containing the *Trichoderma spp.* discussed in this document.

The Agency has determined that the registered uses of *Trichoderma spp*. will "not affect" (NA) endangered or threatened terrestrial or aquatic species as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration (NOAA). However, EPA will review any public comments made in response to this docket and will conduct another risk environmental assessment, if new information makes it appropriate to do so.

State Water Quality Concerns (CWA 303D)

The Agency has determined that dietary exposure to *Trichoderma spp*. via drinking water met the FQPA 1996 safety standard. Moreover, the pesticide active ingredient is not an aquatic fungus and is not likely to percolate through the soil or survive municipal treatment of drinking water.

Trichoderma species are not listed as the cause of impairment for any water bodies 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. The Agency invites submission of water quality data for this microbial. To the extent possible, data should conform to the quality standards in Appendix A of the "OPP Standard Operating Procedure: Inclusion of Water Quality & Impaired Water Body Data in OPP's Registration Review Risk Assessment & Management Process," (see: *http://www.epa.gov/oppsrrd1/registration_review_/water_quality.htm),* in order to ensure that the data can be used quantitatively or qualitatively in pesticide risk assessments.

Incidents

The Agency has not received any adverse reports of human health or environmental incidents in association with these strains of *Trichoderma,* which are pesticide active ingredients.

Efficacy and Label Claims

Efficacy data are not required for the currently registered uses of pesticide products containing *Trichoderma spp*. T-22, T-75 or T-76 because none of the target pests are public health pests.

Labels for the pesticide products in this registration review case 6050 can be obtained by searching on the EPA Registration Number (EPA Reg. No.) on the Pesticide Product Label System (PPLS) website: *http:// oaspub.epa.gov/pestlabl/ppls.home*
The currently registered pesticide products are:

T-22 G Biological Plant Protectant Granules	(EPA Reg. No. 68539-3) - BioWorks
T-22 WP Biological Fungicide	(EPA Reg. No. 68539-4) - BioWorks
Binab™ T Wettable Powder Biorational Fungicide	(EPA Reg. No. 61463-2) - Binab

See **Part IV. List** in this document.

Timeline

EPA has created the following estimated timeline for the completion of the *Trichoderma spp*. 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 *Trichoderma spp.* Docket	April 2007
Close Public Comment Period	June 2007
Develop Final Work Plan (FWP)	August 2007
Open Public Comment Period for Proposed Reg. Review Decision	November
Close Public Comment Period	January 2008
Final Decision	March 2008
Total (years)	1

Guidance for Commenters

The public is invited to comment on EPA's preliminary registration review work plan and rationale. 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 *Trichoderma spp.* case.

Next Steps

After the comment period closes in June 2007, the Agency will prepare a Final Work Plan for this pesticide Registration Review case.

Part II. FACT SHEET - *Trichoderma harzianum* KRL-AG2 ATCC 20847 (or T-22)

Background Information

- *Trichoderma spp*. registration review case number: 6050
- *Trichoderma harzianum* KRL-AG2 ATCC 20847 Rifai (T-22)
- PC Code: 119202; CAS#: 67892-31-3.
- Registrant: BioWorks
- First approved for use in a registered product on November 27, 1990.
- Not subject to reregistration; therefore, no Reregistration Eligibility Decision (RED).
- Original tolerance exemptions for seed treatments on certain food commodities were revised and reassessed in 1999 to include all food commodities and met FQPA 1996 safety standard.
- Biopesticides and Pollution Prevention Division (BPPD), Regulatory Action Leader (RAL), Shanaz Bacchus: bacchus.shanaz@epa.gov

Use Information

- *Trichoderma harzianum* T-22 is used as a fungicide.
- There are two active Section 3 registrations, T-22 G Biological Plant Protectant Granules and T-22 WP Biological Fungicide.
- Label claims control of seed rot, and soil borne plant pathogens and plant root diseases caused by pests such as *Pythium, Rhizoctonia, Cylindrocladium, Fusarium and Thielaviopsis.*
- Used on a variety of sites including commercial seed treatments, greenhouses, nurseries, turf seedlings, some homeowner uses.
- For use at variable rates on a variety of food and non-food crops for commercial seed treatments, in-furrow soil treatments, in greenhouses, nurseries, for transplants and planter boxes, and for application to turf and turf seedlings.

Recent Regulatory Actions

- An exemption from the requirement of a tolerance for residues of *Trichoderma harzianum* Rifai strain KRL-AG2 (ATCC #20847) or T-22 (40 CFR 180.1102; 55 FR 50327) was established on December 6, 1990, for seed treatments of beans (green and dry), cabbage, corn (field and sweet), cotton, cucumbers, peanuts, potatoes, sorghum, soybeans, sugar beets, and tomatoes.
- In 1999 to 2000, the exemption from tolerance was revised and reassessed to include all food/feed commodities (40CFR 180.1102, 64 FR 16856, April 7, 1999; 55 FR 37375; June 14, 2000). This revision and reassessment met the safety standards of FQPA 1996.
- Three of the registered products were canceled (two in 2004 and one in 2006) at the registrant's request by non-payment of maintenance fees.
- Reviews of studies and scientific rationales in requests to waive data for guideline requirements covered product characterization, health and ecological effects. These reviews, public literature, and the low exposure and low toxicity potential of the microbe

support the Agency finding of no harm to health and the environment when T-22 is used as labeled. (See **Part V** of this document).

Human Health Risk Assessment Status

Toxicology

Agency reviews indicate that T-22 is not toxic, infective or pathogenic to rats by oral, pulmonary or intravenous routes of exposure. No incidents of hypersensitivity in humans have been reported to the Agency during the development and use of the products.

- Based on submissions evaluated by the Agency, T-22 ai is in **Toxicity Category IV** for
  - acute oral toxicity/pathogenicity,
  - acute pulmonary toxicity/ pathogenicity,
  - acute intravenous toxicity/pathogenicity, and
  - primary eye irritation

- Based on data and information regarding exposure of manufacturers to T-22, the ai is in **Toxicity Category III** for the following:
  - Acute dermal toxicity/pathogenicity
  - Primary dermal irritation

Dietary (Food and Water)

- The most recent risk assessment September 29, 2004 resulted in unconditional registration of Fafard (EPA Reg. No. 68539-5). This demonstrated that Agency data requirements were met for the labeled uses. It was recently canceled at the request of the registrant in 2006 by non-payment of maintenance fees.
- **April 7, 1999:** The revision and reassessment of the exemption from tolerance for seed treatments on certain crops to include all food/feed commodities ascertained that the pesticide met the FQPA 1996 safety standard. There is no dietary, aggregate, or cumulative exposure which exceeds the Agency's LOC. Based on the low toxicity and low exposure potential, it was not necessary to use a safety factor to assess dietary risks to infants, children, or adults in the US population.
- Subchronic and chronic dietary exposure estimates were not required because toxicology data for Tier I studies were acceptable and did not trigger Tier II and Tier III data.
- The Agency concluded that residues of *Trichoderma harzianum* T-22 are not likely to pose a risk in drinking water. Both percolation through soil and municipal treatment of drinking water would reduce the possibility of exposure to *Trichoderma harzianum* T-22 via drinking water.
- There are no dietary risks that exceed the Agency's LOC.

Residential

- There are no residential risks that exceed the Agency's LOC.

Occupational

- There are no occupational risks that exceed the Agency's LOC.

Tolerances

- An exemption from tolerance for residues in 40 CFR 180.1102 on all food/feed commodities met the FQPA 1996 safety standard (see **Recent Regulatory Actions** in this document).

Ecological Risk Assessment Status

- Acute risks to non-target organisms (birds, wildlife, vertebrates, invertebrates and insects) are unlikely to exceed the Agency's level of concern (LOC).
- T-22 is used to protect plant roots from soil borne pathogens. The use sites and application methods pose a low exposure scenario to a pesticide with low toxicity potential.
- Tier I data are acceptable and did not trigger chronic risk assessments.

Endangered Species Considerations

- *Trichoderma harzianum* T-22 is an antagonist of plant pathogenic fungi. It has no comparable activity on vertebrate, invertebrate or plant species. In addition, there is no evidence of toxicity to listed threatened or endangered species and/or effects on critical habitat based on data obtained from guideline studies and/or a review of the available literature. As a result, the Agency has determined that the registered uses of *Trichoderma harzianum* T-22 will "Not affect" (NA) endangered or threatened terrestrial or aquatic species as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration (NOAA).

Data Call-In Status

- At this time, there is no data call in issued for *Trichoderma harzianum* T-22.

Labels

- A list of registration numbers may be found in the *Trichoderma spp.* docket (see **Part IV. List** in this document). The labels can be obtained from the Pesticide Product Label System (PPLS) website: *http://oaspub.epa.gov/pestlabl/ppls.home* by searching on the EPA Registration Number (EPA Reg. No.). Pesticide products, each containing 1.15 percent of T-22, are:
  T-22 G Biological Plant Protectant Granules (EPA Reg. No. 68539-3) - BioWorks, Inc.
  T-22 WP Biological Fungicide (EPA Reg. No. 68539-4) - BioWorks, Inc.

III. FACT SHEET: *Trichoderma polysporum* (ATCC 20475) *Trichoderma viride* (ATCC 20476)

Background Information

Trichoderma spp. registration review case number: 6050

- *Trichoderma polysporum* (ATCC 20475) - called T-75
- PC Code 128902)
- *Trichoderma viride* (ATCC 20476) - called T-76
- PC Code 128903
- CAS# 67892-34-6
- Technical registrant: BINAB™ USA, Inc
- First approved for use in a registered product on July 24, 1989.
- Not subject to reregistration (no Reregistration Eligibility Decision (RED)
- Non-food use - no numerical tolerance or exemption from tolerances.
- Biopesticides and Pollution Prevention Division (BPPD), Regulatory Action Leader (RAL), Shanaz Bacchus; email: bacchus.shanaz@epa.gov

Use Information

- *Trichoderma polysporum* (ATCC 20475) and *Trichoderma viride* (ATCC 20476) are combined active ingredients in **one** currently registered Section 3 pesticide product, Binab™ T Wettable Powder Biorational Fungicide (EPA Reg. No.61463-2) (see **Part IV. List** in this document).
- The End-use Product (EP) is a wettable powder (WP) formulation, registered for use in the control of decay of pruning wounds of ornamental, shade, and forest trees.
- **Not** for trees bearing fruits to be used as food commodity, since there is no exemption from tolerance established for these strains.
- Pests controlled are fungi which cause decay in tree wounds – *Heterobasidion annosum, Chodrostereum purpureum.*
- The label specifies that one part of the WP is to be mixed with two parts drinking quality water (w/v) and applied to the wound with a paint brush. It must be applied within two hours of mixing. A recommended tree wound sealant, which does not contain a fungicide, is applied immediately after the Binab™ T Wettable Powder application.

Recent Regulatory Actions

- Another pesticide product, Binab™ T Pellets Biorational Fungicide, containing T-75 and T-76 (EPA Reg. No. 61463-1), was previously registered in 1989 for use in the control of internal decay of wood utility poles, playground structures and fence posts. It was canceled at the registrant's request in 1991 by non-payment of maintenance fees.

Human Health Risk Assessment Status

Toxicology

- Toxicity Category IV based on review of acute oral and subcutaneous studies for both parent microbes (LD_{50} >1,000 mg/kg)

- Toxicity Category IV acute oral and subcutaneous LD_{5O} toxicities in mice for the potential metabolite, trichodermin, an antibiotic, were greater than 1,000 mg/kg and 500-1,000 mg/kg respectively.

Dietary (Food and Water)

- These are non-food use pesticide active ingredients.
- The Agency does not expect any risk from drinking water exposed as a result of the use of these active ingredients based on their low exposure and low toxicity potential.

Residential

- Risks from residential uses of these active ingredients do not exceed the Agency's LOC.

Occupational:

- There are no occupational risks that exceed the Agency's LOC.

Tolerances

- There is no numerical tolerance or an exemption from tolerance for these active ingredients.

Ecological Risk Assessment Status

- Data on the ecological characteristics of the products were waived based on the inability of the fungi to grow at or near body temperatures of mammals or birds. The fungi are ubiquitous soil organisms and do not grow in water. The use patterns are unlikely to result in additional exposure of ecological concern to aquatic organisms or other non-target wildlife.
- No further ecological or environmental fate data are required for the labeled uses.

Endangered Species Considerations

- *Trichoderma polysporum* (ATCC 20475) and *Trichoderma viride* (ATCC 20476) are antagonists of plant pathogenic fungi. They have no comparable activity on vertebrate, invertebrate or plant species. In addition, there is no evidence of toxicity to listed threatened or endangered species and/or effects on critical habitat based on data obtained from guideline studies and/or a review of the available literature. As a result, the Agency has determined that the registered uses of *Trichoderma harzianum* T-22 will "Not affect" (NA) endangered or threatened terrestrial or aquatic species as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration (NOAA).

Data Call-In Status

- At this time, there is no data call-in issued for *Trichoderma polysporum* and *Trichoderma viride*, T-75 and T76, respectively.

Labels

- A list of registration numbers may be found in the *Trichoderma spp.* docket (see **Part IV**. **List** in this document). The labels can then be obtained by searching on the EPA Registration Number (EPA Reg. No.) on the Pesticide Product Label System (PPLS) website: *http://oaspub.epa.gov/pestlabl/ppls.home* The single registered pesticide containing 16.6 percent each of T-75 and T-76 is:
  Binab™ T Wettable Powder Biorational Fungicide (EPA Reg. No.61463-2) - Binab.

Part IV. List of Products containing *Trichoderma spp.*

***Trichoderma harzianum* KRL-AG2 or T-22**

EPA Reg. No.	Product Name	First registered Date
68539-3	T-22 G Biological Plant Protectant Granules	05/21/1993
68539-4	T-22 WP Biological Fungicide	05/21/1993

Registrant:
BioWorks Inc.
122 North Genesee Street
Geneva, New York 14456
Five products were registered between 1990 and 2005. Three were canceled between 2004 and 2006. Registrations of the two active products above are based on acceptable data submitted for the 1990 registrations.

***Trichoderma polysporum* and *Trichoderma viride* (T-75 and T-76)**

EPA Reg. No.	Product Name	First registered Date
61463-2	Binab™T Wettable Powder Biorational Fungicide	07/24/1989

Registrant:
BINAB™ USA, Inc.
3rd Floor, 214 West Mifflin Street
Madison, WI 53703-2594
Two products, containing the combined strains T-75 and T-76, were registered in 1989. One pesticide product was canceled in 1991. The remaining product shown above contains 16.6 percent of each strain and inert ingredients.

Part V: Supplementary Information about *Trichoderma harzianum* KRL-AG2 (called T-22)

United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7511P)

1. DESCRIPTION OF THE BIOLOGICAL PESTICIDE

Generic Name(s) of the Active Ingredient(s): *Trichoderma harzianum* Rifai Strain KRL-AG2 called T-22

OPP Chemical Codes: 119202
Year of Initial Registration: 1990
Pesticide Type: Biofungicide

U.S. and Foreign Producers: Bioworks, Inc.
122 North Genesee Street
Geneva, New York 14456

2. USE SITES, APPLICATION TIMING & TARGET PESTS

Target Pests: Label claims control of seed rot and soil borne plant pathogens and plant root diseases caused by pests such as *Pythium, Rhizoctonia, Cylindrocladium, Fusarium and Thielaviopsis.*

Registered Uses: For use as commercial seed treatments; on cuttings; nursery drench; in greenhouses; in-furrow spray and soil treatment; shade house and nursery crops; greenhouse and nursery planting mix amendment; greenhouse and nursery drench; greenhouse foliar spray; greenhouse chemigation; home and garden drench; planter box (on-site); transplant starter; potting soil; broadcast to established turf; new turf seedlings. The pesticide can be used on all food/feed commodities **except sugarcane, pechay (bok choy), rice, mushrooms, kiwi, tobacco, barley, oats, lemon, apple, and chickpea. Not for use on aquatic crops.**

3. FOOD CLEARANCES / TOLERANCES

An exemption from the requirement of a tolerance for residues of *Trichoderma harzianum* Rifai strain KRL-AG2 (ATCC #20847) or Strain T-22 (40 CFR 180.1102) was

established on December 6, 1990, for seed treatments of beans (green and dry), cabbage, corn (field and sweet), cotton, cucumbers, peanuts, potatoes, sorghum, soybeans, sugar beets, and tomatoes. This tolerance exemption was later revised and reassessed to include all food/feed commodities (40CFR 180.1102, 64 FR 16856, April 7, 1999; 55 FR 37375; June 14, 2000), and found to meet the FQPA 1996 safety standard. The exemption applies when *Trichoderma harzianum* Rifai strain KRL-AG2 or T-22 is applied as a fungicide at approved label rates and on sites as described on the label for the registered pesticide product. The BBPD website (*http://www.epa.gov/pesticides/biopesticides*) provides additional information on this and other biopesticide active ingredients.

4. SCIENCE FINDINGS

A. PRODUCT CHEMISTRY

All product chemistry requirements have been met and sufficient analytical methodology exists to maintain quality control of the pesticide products. All batches containing unintentional ingredients of toxicological concern are to be destroyed.

B. TOXICOLOGY

Reviews of the following toxicity studies meet the safety standards of FQPA 1996. All studies were classified as acceptable. The review of these studies indicated that the biofungicide is not toxic to, infective in, or pathogenic to rats by oral, pulmonary or intravenous routes of exposure.

Acute Toxicity/Pathogenicity

The toxicological studies listed below were evaluated for registration of this active ingredient. The data submitted to support the initial registration of this product include: acute toxicity/pathogenicity studies in rats to demonstrate oral, pulmonary, and intravenous effects, and a primary eye irritation study in rabbits. The active ingredient is classified as toxicity category IV on the basis of those studies. A request to waive data was granted for acute dermal toxicity guideline requirement. The active ingredient is classified as Toxicity Category III for acute dermal toxicity/pathogenicity and primary dermal irritation, based on the nature of the pesticide and worker exposure during its manufacture.

1. Acute oral toxicity/pathogenicity (Toxicity Category IV): No apparent signs of treatment-related toxicity, infectivity or pathogenicity were observed in male and female rats either early post dosing or during the 21-day test period. Both treated and control animals demonstrated weight gains. The test material was cleared from the gastrointestinal tract by Day 2 of the study.

2. Acute pulmonary toxicity/pathogenicity (Toxicity Category IV): No signs of treatment-related toxicity were observed when male and female rats were each treated with a single intratracheal instillation of 10^8 cfu/0.04 ml per animal. Following instillation, the test

organism was detected predominantly in the lungs of treated animals on Day 1, but was reduced by Day 14. Clearance of *T. harzianum* occurred by Day 21.

3. Acute intravenous toxicity/pathogenicity (Toxicity Category IV): A single intravenous injection at 10^7 cfu of *T. harzianum* KRL-AG2 per animal did not produce any apparent signs of toxicity or pathogenicity to rats following a 21 day test period. A distinct pattern of clearance was observed within the 21 day test period, with the lungs of treated animals showing traces of the test microbe. Enlarged spleens, which were observed in 9 of the 15 treated animals, were considered to be the result of the organ's involvement in the clearance of T-22 from the blood. No evidence of pathogenicity was observed.

4. Acute dermal toxicity: A request that acute dermal toxicity testing be waived for this biofungicide was made based on the ubiquitous occurrence of *Trichoderma spp.* To support the waiver, the registrant provided additional information on the history of the production process, and worker exposure (including a summary of sources of operator exposure and the number of exposure hours for a typical employee involved in the manufacturing process). The major potential source of worker exposure occurred during the fermentation process. The registrant stated that during manufacture no workers have shown evidence of dermal sensitivity or adverse effect to F-Stop, which contains T-22. Based on this information and the results of the acute oral, pulmonary and intravenous studies, the Agency waived the acute dermal toxicity test, and categorized the active ingredient as Toxicity Category III.

5. Primary dermal irritation: The pesticide was placed in Toxicity Category III based on the nature of the active ingredient and the inert ingredients, and the previously discussed report of worker exposure (see Acute dermal toxicity).

6. Primary eye irritation: *Trichoderma harzianum* strain T-22 at 0.1 gram or 10^8 cfu per eye initially caused slight irritation to rabbit eyes but no irritation was noted by day 7 of the observation period. The pesticide was considered Toxicity Category IV for primary eye irritation.

7. Hypersensitivity: No incidents of hypersensitivity in humans have been reported during development of the products. To date, the Agency has not received any reports of hypersensitivity or adverse effects during the time T-22 has been used as a pesticide. As with all pesticides, any incidents of hypersensitivity or adverse effects must be reported to the Agency to comply with 6(a)(2) requirements.

Genotoxicity, reproductive and developmental toxicity, subchronic toxicity, and chronic toxicity.

These studies were not required based on the lack of acute toxicity/pathogenicity in the Tier I studies. During simulated use conditions, strain T-22 produces no known metabolites of environmental or health concern. This organism controls plant disease by competing with plant pathogens for root and foliar surfaces for the establishment of fungal colonies and by

mycoparasitism. There are no known genotoxic or reproductive effects as a result of mammalian exposure to this strain.

C. FOOD QUALITY PROTECTION ACT REQUIREMENTS

No unreasonable adverse effects to human health are expected from the use of *Trichoderma harzianum* KRL-AG2 when used as labeled. An exemption from the requirement of a tolerance has been established under Section 408(c)(2)(A)(I) of the Federal Food, Drug, and Cosmetics Act. The Agency has assessed the toxicology data base for *Trichoderma harzianum* Rifai strain KRL-AG2 in light of the safety factors listed in FQPA 1996 and has concluded with reasonable certainty that the proposed uses of this microbial insecticide do not pose aggregate and/or cumulative risks to the general US population, including infants and children.

Human Health Effects

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

Dietary exposure to the microbial pesticide is likely to occur. The lack of acute oral toxicity/pathogenicity due to the ubiquitous nature of the microbial and based on the acute oral toxicology test in rats, support the exemption from the requirement of a tolerance for this active ingredient.

a. Food.

The microbial pesticide can be removed from foods by washing, peeling, cooking and processing. Even if ingested, the low acute oral toxicity Category IV potential indicates minimal risk. Consequently, dietary exposure to the microbial and the risk posed by ingestion of foods treated with the microbial pesticide, are likely to be minimal for adults, infants and children by the oral route.

b. Drinking Water Exposure and Risk Characterization

The microorganism *Trichoderma harzianum* KRL-AG2 is common in the soil. It is not known as an aquatic microorganism, and therefore is not expected to proliferate in aquatic habitats. Drinking water is not being screened for *Trichoderma harzianum* KRL-AG2 as a potential indicator of microbial contamination. Both percolation through soil and municipal treatment of drinking water would reduce the possibility of exposure to *Trichoderma harzianum* KRL-AG2 through drinking water. Therefore, the potential of significant transfer to drinking water is minimal to nonexistent. However, even if negligible oral exposure should occur through drinking water, the Agency concludes that such exposure would present no risk due to the lack of mammalian toxicity, the inability of the microbe to grow at mammalian body temperature, and the ubiquitous nature of the microbe.

2. Common Mode of Action

There is no other strain of *Trichoderma harzianum* registered at this time. Other species of the fungal genus *Trichoderma* are also registered with a history of safe use. EPA does not believe that there is any concern regarding the potential for cumulative effects of the currently

registered strain of *Trichoderma harzianum* T-22 due to a common mechanism of toxicity. The toxicology studies performed on registered *Trichoderma spp.* demonstrate a low toxicity potential for each fungal strain.

3. Risks Posed by Potential Residential, School or Daycare Exposure

Exposure and risk to adults, infants and children via treated lawns or recreational areas are likely if the pesticide is used as labeled. However, the pesticide is a naturally occurring microbe and is ubiquitous in the environment. Based on the low toxicity potential as evidenced by the data submitted, the microbial pesticide active ingredient is likely to pose a minimal to non-existent risk if used as labeled.

4. 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 microbial 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/pathogenicity potential as demonstrated by the studies submitted in support of the registration of both the technical Grade Active Ingredient (TGAI) and the End-use Products (EPs). Aggregate exposure and risk to registered strains of *Trichoderma harzianum* is an ongoing assessment as products seek registration.

5. Safety Factors

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database unless EPA determines that a different margin of exposure (safety) will be safe for infants and children. In this instance, EPA believes there are reliable data to support the conclusion that there are no threshold effects of concern to infants, children and adults when *Trichoderma harzianum* KRL-AG2 (T-22) is used as labeled. As a result, the provision requiring an additional margin of exposure does not apply.

6. Determination of Safety for U.S. Population, Infants and Children

There is a reasonable certainty that no harm will result from aggregate exposure to the U.S. population, including infants and children, to *Trichoderma harzianum* KRL-AG2 (T-22) from the use pattern of this microbial pesticide. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

7. Other Considerations

a. Endocrine Disruptors and Immune Response

Additional data specifically on the endocrine effects of this microbial pesticide are not required at this time. However, the Agency has considered, among other relevant factors, available information concerning whether this microorganism may have an effect in humans similar to an effect produced by a naturally occurring estrogen or other endocrine effects. At this time, there is no information indicating that *Trichoderma harzianum* KRL-AG2 or T-22 produces a metabolite that may be an endocrine disruptor. As expected from a non-pathogenic microorganism, the submitted toxicity/pathogenicity studies in the rodent (required for microbial

pesticides) indicate that following several routes of exposure, the immune system is still intact and able to process and clear the active ingredient. Therefore, no adverse effects to the endocrine or immune systems are known or expected.

b. Analytical Method(s)

The registrant has submitted data in support of the Agency requirements to identify the active ingredient and potential metabolites and unintentional ingredients. Analytical methods are available and sufficient to maintain quality control of products containing *T. harzianum* strain T-22. All batches containing potential human pathogens and unintentional ingredients of toxicological concern must be destroyed.

D. OCCUPATIONAL AND RESIDENTIAL EXPOSURE AND RISK

There is likely to be occupational and residential exposure and risk to the microbial pesticide from the proposed uses as seed treatments and from ground applications to agricultural crops, ornamentals, turf and greenhouses.

1. Dermal exposure and risk. Workers are most likely to be dermally exposed during treatment of all registered sites which include food commodities. Because the pesticide demonstrated no acute dermal effects on employees who manufacture the products, and it is widely distributed in nature, the exposure and risk to workers is likely to be minimal if appropriate recommended Personal Protective Equipment is used as labeled. Where the Agency has required Restricted Entry Intervals (REIs), early entry workers may enter treated fields if wearing appropriate Personal Protective Equipment as indicated on the registered labels.

2. Inhalation exposure and risk. The pesticide is considered an acute Toxicity Category IV microbial pesticide on the basis of acute pulmonary studies. Based on this low toxicity/pathogenicity potential and because inhalation exposure is not usually as great as dermal exposure to workers, the Agency believes that the use of products containing this active ingredient is not likely to pose an undue risk to workers. When necessary, adequate Restricted Entry Intervals and the use of Personal Protective Equipment, including a respirator with NIOSH approval prefix N-95, P-95 or R-95, are required to mitigate against potential exposure and risk posed to pesticide handlers and workers.

E. ENVIRONMENTAL ASSESSMENT AND RISK

The microbial active ingredient is a naturally occurring ubiquitous fungus, which is found in soils. It is not known to proliferate in aquatic habitats. Based on its low toxicity potential, and low exposure potential, it is not likely to pose any undue hazard to the environment.

F. ECOLOGICAL EFFECTS

1. Avian Oral Toxicity/Pathogenicity Studies in the Northern Bobwhite: An avian oral toxicity/pathogenicity study on bobwhite quail was evaluated by the Agency. A dose of 2222

mg/kg bird weight was administered to the test animals for 5 days for a total dose of 11,110 mg/kg bird weight or approximately 4 x 10^9 cfu/kg bird weight. None of the birds died 30 days after dosing. The LD_{50} was considered to be greater than 11,110 mg/kg bird weight. This test indicated that *Trichoderma harzianum* Rifai strain KRL-AG2 is practically nontoxic to terrestrial avian species by ingestion. The requirement for tests on aquatic birds was waived because it is not expected that the fungus will enter the aquatic environment.

2. Honeybee Acute Toxicity/Pathogenicity: Exposure of the honeybee to *T. harzianum* strain KRL-AG2 (T-22) from agricultural applications is likely to be minimal. The approved methods of application do not include foliar applications to crops in fields. Rather the pesticide is to be used mainly in nurseries, shade houses, greenhouses, and planter boxes and applied to the soil as in-furrow treatments. These agricultural use patterns are likely to minimize exposure to honey bees. Moreover, T-22 is a not an insect pathogen and, therefore, is not expected to harm honey bees.

Data Waivers Granted:

The following data waivers were granted for the reasons listed below each guideline requirement. Also, no toxins or antibiotics were produced in simulated use conditions and batches containing any unintentional ingredients of toxicological concern must be destroyed. In addition, the microbe is ubiquitous and the inert ingredients in the end-use products were cleared for food use for the approved application methods.

1. Acute dermal toxicity: No workers have shown evidence of dermal sensitivity to the organism, and at other steps in the manufacturing process no indication of adverse effects were shown (see **Acute Toxicity/Pathogenicity Unit 4.B.4**. discussion above).

2. Avian Inhalation Testing: This study was not required because this fungus does not typically grow at normal bird body temperatures. In addition, the avian oral toxicity/pathogenicity study in northern bobwhite quail with the Technical Grade Active Ingredient, *T. harzianum* Strain KRL-AG2, fulfilled all avian data testing requirements.

3. Wild Mammal Testing: This testing requirement has been waived because this fungus does not typically grow at normal mammalian temperatures or at temperatures greater than 24^0C. In addition, acute toxicity/pathogenicity tests in rodents, as discussed herein, indicate that T-22 will not harm mammals.

4. Freshwater Fish and Aquatic Invertebrates (including estuarine and marine organisms): Data requirements for evaluating adverse effects on freshwater fish and aquatic invertebrates, estuarine and marine organisms were waived for the original seed treatment applications. For the extension of ground applications to all agricultural crops, the Agency relied on the public literature and reports from the company on the effects of *Trichoderma* on the non-target organisms. T-22 is a soil organism and is not expected to proliferate in aquatic environments. Nevertheless, the Agency did not allow direct applications to water or to crops grown in water.

5. Non-target Insects: Exposure to non-target insects is expected to be minimal to non-existent from the labeled methods of application (in-furrow soil treatments, greenhouse and nursery applications). Moreover, T-22 is not an insect pathogen. No further data are required for the labeled application methods and sites.

6. Nontarget Plant Testing, Guideline 154A-22: The Agency has decided that the pesticide cannot be used on sugarcane, pechay (bok choy), rice, mushrooms, kiwi, tobacco, barley, oats, lemon, apple, and chickpea, because the registrant did not provide data to support application to these sites. In addition, T-22 is not registered for use on aquatic crops.

G. ECOLOGICAL RISK ASSESSMENT

This microbial active ingredient occurs ubiquitously in the environment. It demonstrates a low toxicity profile, and potential exposure is limited by the types of soil applications and approved label rates and sites. Based on these factors and the data submitted, no adverse ecological risks are expected as a result of exposure to this microorganism, if it is used as labeled.

H. SUMMARY OF DATA GAPS

There are no data gaps for the currently registered sites.

5. REGULATORY ACTIONS

There is a reasonable certainty of no harm to human adults, infants and children, other non-target organisms and the environment as a result of the use of pesticide products containing *Trichoderma harzianum* Rifai strain KRL-AG2 (T-22). The active ingredient was first registered on November, 1990. The Agency considered the availability of a biological fungicide would provide a less toxic alternative to the currently registered chemical seed treatments. A discussion of the data evaluated to revise and reassess the exemption from tolerance to meet the FQPA 1996 safety standard is discussed herein. Three of the five registered products have been canceled between 2004 and 2006 at the request of the registrant by non-payment of maintenance fees.

6. LABEL REQUIREMENTS

All labels must meet Agency requirements for pesticide labeling.

7. CONTACT PERSON AT EPA **Office location/telephone number**

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DISCLAIMER: The information provided herein is a summary only and is not to be used to satisfy data requirements for pesticide registration and reregistration. Contact the Product Manager listed above for further information.

VI Website addresses

http://www.epa.gov/oppsrrd1/registration_review/

http://www.epa.gov/oppfead1/labeling/lrm/chap-07.htm

http://www.epa.gov/oppfead1/labeling/lrm/chap-07.htm

http://www.epa.gov/pesticides/biopesticides

http://oaspub.epa.gov/pestlabl/ppls.home

http://oaspub.epa.gov/tmdl/waters_list.impairments? p_impid=3

http://www.epa.gov/oppsrrd1/registration_review_/water_quality.htm