US Environmental Protection Agency
Office of Pesticide Programs

BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Lysophosphatidylethanolamine (LPE) (PC Code 105120)

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U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
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BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

Office of Pesticide Programs:

Biopesticides and Pollution Prevention Division

Biochemical Pesticides Branch

Sheryl K. Reilly, Ph.D.	Biologist, Branch Chief
Freshteh Toghrol, Ph.D.	Chemist, Senior Scientist
Linda Hollis	Microbiologist, Team Leader
Russell S. Jones, Ph.D.	Biologist, Health Effects/Nontarget Organisms
Carol E. Frazer, Ph.D.	Toxicologist, Regulatory Action Leader

I. Executive Summary

A. IDENTITY

The technical grade active ingredient (TGAI) consists of 94% lysophosphatidylethanolamine (LPE), a natural constituent of all living cell membranes, created when phosphatidylethanolamine is broken down by a phospholipase. Fifty percent of the membrane is phospholipid and the LPE is one to ten percent of the lipid content of the cell, depending on cell type. The end-use product, LPE-94 10% Aqueous Growth Regulator, contains 10% LPE.

B. USE/USAGE

LPE-94 10% Aqueous Growth Regulator is a pre-harvest spray for use on various fruit and vegetable crops to enhance ripening mechanisms. The product may also be used in a post-harvest bath application to increase the shelf life of fruits, vegetables and cut flowers. The use is classified as a food crop application.

C. RISK ASSESSMENT

No unreasonable adverse effects on humans or the environment are anticipated from aggregate exposure to LPE-94 10% Aqueous Growth Regulator. This includes all anticipated exposures for which there is reliable information.

1. Human Health Risk Assessment

a. Toxicological Endpoints

No toxicological endpoints were identified. Mammalian toxicology data requirements were submitted and adequately satisfy data requirements to support the registration. Submitted data for the TGAI and the end-use product indicate Toxicity Category IV for acute oral and acute inhalation toxicity. Acute dermal toxicity data is represented by a Toxicity Category III as the limit dose tested, only 2,000 mg/kg, had no toxic effects. The data reported for primary eye irritation studies showed that the test substance was minimally irritating, and is thus a Toxicity Category III when the TGAI is used and Toxicity Category IV when the end use product is used as the test material. Exposure to either the TGAI or the end-use product produced no skin irritation in animal tests; as a result, a Toxicity Category IV is given for dermal irritation. Both the Technical and end-use products are significant dermal sensitizers.

b. Human Exposure

Exposure to the general population would be low but worker exposure is expected. Appropriate protective wear and precautionary label language will mitigate vulnerability.

c. Risk Assessment

The Biopesticides and Pollution Prevention Division (BPPD) has not identified any subchronic, chronic, immune, endocrine, dietary or nondietary exposure issues with respect to LPE as relates to children or the general U.S. population. Dermal sensitization risk to applicators is mitigated providing label directions are followed. No toxicological endpoints have been identified, and there is limited exposure of the general public to this product when used according to the label instructions. The Agency has considered LPE in light of relevant safety factors in the Food Quality Protection Act (FQPA) of 1996 and under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and determined there will be no unreasonable adverse effects from the use of this product.

2. Ecological Risk Assessment

a. Ecological Toxicity Endpoints

The data requirements for ecological testing were waived because no toxic endpoints were identified from the submitted mammalian data or literature review.

b. Ecological Exposure

The active ingredient is a natural constituent found in biological organisms. Sprayed LPE residues are low, and are reduced further by catabolism through the lipid metabolic system found in most organisms.

c. Risk Assessment

Risk to other organisms is expected to be minimal due to the low chances of exposure to the environment. Moreover, the active ingredient is a metabolic degradation product of most biological entities. BPPD posits LPE used according to label directions will not result in significant adverse effects to wildlife or other organisms.

D. DATA GAPS / LABELING RESTRICTIONS

There are no data gaps or labeling restrictions. Because of LPE's Toxicity Category III for dermal toxicity, some restrictions and precautionary labeling are required to mitigate risks associated with proposed uses (see Labeling Rationale for details).

II. Overview

A. ACTIVE INGREDIENT OVERVIEW

Common Name: LPE

Chemical Name: Lysophosphatidylethanolamine

CAS Number: 95046-40-5

Trade and Other Names: LPE E94T; LPE-94 10% Aqueous; phospholipid; lyso-PE

OPP Chemical Code: 105120

Basic Manufacturer: Nutra-Park, Inc.
8383 Greenway Boulevard, Suite 520
Middleton, WI 53562

B. USE PROFILE

Proposed uses and application methods for LPE include the following:

Type of Pesticide: Growth Regulator

Use Sites: LPE is approved for field use on any type of agricultural commodity, for storage of harvested crops and on cut flowers.

Formulation Types: Liquid

Method and Rates of Application: Conventional spray application equipment should be used in the field. Shake LPE-94 10% Aqueous product well (1-3 min.) before mixing with water. Into half the desired amount of water, add the shaken LPE and then the remaining water for intended crop. The maximum concentration is 1 gallon (0.1 gallon of the active ingredient) per 100 gallons of spray solution (400 ppm LPE).

When used for post-harvest treatment, raw agricultural commodities are dipped into or sprayed with a solution containing 25-100 ppm LPE and air dried prior to storage. For cut flowers, apply 25-50 ppm LPE in the storage solution.

Use Practice Limitations: Do not allow workers into treated areas for four hours following application.

Timing: Application in the field should start at 20 to 30 days before first harvest, depending on crop. Repeat at 7 to 10 day intervals.

C. ESTIMATED USAGE

The Experimental Use Permit (EUP) in 2001 allowed application over 2,475 acres in 10 states with a maximum concentration of 500 ppm LPE.

D. DATA REQUIREMENTS

BPPD reviewed data requirements for granting this registration under Section 3(c)(5) of FIFRA. Mammalian toxicology and ecological effects data requirements for LPE were fulfilled. Product analysis data requirements are adequately satisfied.

E. REGULATORY HISTORY

On July 18, 1997, EPA received an application from JP BioRegulators, Inc. for an Experimental Use Permit (EUP) covering the use of lysophosphatidylethanolamine to enhance ripening and extend storage time. On September 25, 1998, the Agency granted the EUP (63 FR 51352) to use 72 kilograms/year of the biochemical phospholipid: Lyso-PE (lysophosphatidylethanolamine) on 570 acres of apples, citrus, cranberries, grapes, nectarines, peaches, pears, strawberries, and tomatoes in nine states at a concentration of 100-500 ppm active ingredient. This was to evaluate ripening and storage shelf life. On June 2, 2001, three additional crops, blueberries, cherries and peppers, were added to the exemption from the requirement for a tolerance. The EUP was extended to include 2,475 acres in 10 states for two years at a rate of 12-500 ppm active ingredient (66 FR 39648).

On November 21, 2000, the Agency received an application for two new products with the new active ingredient, lysophosphatidylethanolamine. A notice of receipt of the application for registration of Lysophosphatidylethanolamine was published in the Federal Register on 19 September 2001 (66 FR 48256) with a 30-day comment period. No comments were received following this publication.

On January 3, 2001, EPA published a Notice of Filing Petition to Establish an Exemption from the Requirement of a Tolerance (67 FR 323) with a 30-day comment period. No comments were received.

F. CLASSIFICATION

In 1995, the Biochemical Classification Committee determined that LPE is a biochemical pesticide, a plant growth regulator, because it is naturally occurring with a non-toxic, indirect mode of action.

G. FOOD CLEARANCES/TOLERANCES

On June 12, 1998 (63 FR 32134), Phospholipid: Lyso-PE (lysophosphatidylethanolamine) was exempted from tolerance, on a temporary basis, until June 1, 200l. On August 1, 2001 (66 FR 39648), the temporary exemption was extended to June 1, 2003. On January 3, 2001, EPA published a Notice of Filing Petition to Establish an Exemption from the Requirement of a Tolerance (67 FR 323) with a 30-day comment period. No comments were received. A final rule establishing an exemption from the requirement of a tolerance is being published associated with this document. There are no Codex tolerances for lysophosphatidylethanolamine.

III. Science Assessment

A. PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT

All product chemistry data requirements for the technical grade and the end-use products are met.

1. Product Identity and Mode of Action

a. Product Identity:

The technical grade active ingredient, LPE E94T consists *of 94% LPE and the end-use product, LPE-94 10% Aqueous Growth Regulator, 10% LPE.*

b. Mode of Action:

The precise mode of action is unknown, but LPE has been shown to enhance ripening and extend the shelf life of certain fruits by increasing ethylene production without increasing respiration. It has also been shown to inhibit senescence of ornamental flowers by inhibiting ethylene production and the activity of certain phospholipase enzymes.

2. Physical And Chemical Properties Assessment

The physical and chemical characteristics of the TGAI and the end-use product were submitted to support the registration. They are summarized in Table 1.

Table 1. Product chemistry data requirements:

Product Chemistry	TGAI/MP (MRID 454357-02)	EP (MRID 452736-06)
151B-10 (880.1100): Product identity	LPE E94T, the technical product, consists of 94% lysophosphatidylethanolamine and 6% impurities	LPE-94 10% Aqueous, the end-use product, contains 10% lysophosphatidylethanolamine
151B-11 (880.1620): Formulation process	An acceptable description of the manufacturing process was submitted.	The product is formulated via a simple mixing process without any chemical reactions.
151B-12 (880.1400): Discussion of formulation of unintentional impurities	Acceptable nominal concentrations and certified limits were reported for the manufacturing impurities.	No impurities of toxicologic concern are formed during the formulation process.
151B-13 (880.1700): Preliminary analysis	Data obtained from the five-batch analysis demonstrate that the analytical method is precise and accurate. (MRID 452740-06)	No five-batch preliminary analysis data were submitted, but none are required since the end-use product is not manufactured via an integrated system, and because the TGAI/MP will be registered simultaneously with the EP.
880.1750: Certified limits	The certified limits for the active ingredient and other impurities are acceptable.	Acceptable nominal concentrations and certified limits were reported for the other (inert) ingredient in the formulation.
880.1800: Enforcement analytical method	The analytical method is HPLC with an evaporative light scattering detector (ELSD).	An acceptable HPLC/ELSD analytical method was submitted.
Physical/Chemical Properties	**TGAI/MP (MRID**	**EP (MRID 454361-03)**
880.6302: Color	Off white to yellow	Off white to faint yellow
880.6303: Physical State	Fine powder (solid)	Suspension
880.6304: Odor	Faint lipid (vegetable oil) aroma	Faint characteristic odor of lipid (vegetable oil)

Product Chemistry	TGAI/MP (MRID 454357-02)	EP (MRID 452736-06)
880.7200: Melting Point	Melts over a range of temperatures (MRID 4444534-01)	N/A, not a solid
880.7220: Boiling Point	N/A, not a liquid	Not required under 40 CFR §158.190
880.7300: Density, Bulk Density, or Specific Gravity	Approximately 1 g/cc	~1.2 g/cc^3 (MRID 443399-02)
880.7840: Solubility	Forms micelles in water	Not reported, but required for TGAI under 40 CFR §158.190
880.7050: Vapor Pressure	< 2.1 x 10^{-4} Pa at 25°C (MRID 452740-07)	Not required for EP
880.7370: Dissociation constant	N/A, does not dissociate	N/A, does not dissociate
880.7550: Octanol/water partition coefficient	log P_{ow} > 6.2 (MRID 452740-07)	Not required for EP
880.7000: pH	6-8	6.5-7.0
Stability	Over an extended period of time the unsaturated acyl chains will slowly oxidize (MRID 4444534-01)	Not reported, but required for TGAI under 40 CFR §158.190
880.6314: Oxidizing or Reduction Action	N/A, does not contain an oxidizing or reducing agent	N/A, does not contain an oxidizing or reducing agent.
880.6315: Flammability/Flame Extension	N/A, is not a combustible liquid.	N/A, is not a combustible liquid.
880.6316: Explodability	N/A, is not a potential explosive.	N/A, does not contain explosive material.
880.6317: Storage Stability	Stable at -20°C for 6 months	Interim reports show the end-use formulation is stable for more than 30 days under normal storage conditions.
880.7100: Viscosity	N/A, is not a liquid.	7.3 cps (at 60 rpm) at 20°C 6.2 cps (at 60 rpm) at 40°C
880.6319: Miscibility	N/A, is not an emulsifiable liquid.	N/A, is not to be diluted with petroleum solvents.

Product Chemistry	TGAI/MP (MRID 454357-02)	EP (MRID 452736-06)
880.6320: Corrosion Characteristics	Non-corrosive	Non-corrosive
880.6321: Dielectric Breakdown Voltage	N/A, is not a liquid used around electrical equipment	N/A, is not to be used around electrical equipment

B. HUMAN HEALTH ASSESSMENT

Information submitted to support the registration application of the technical grade active ingredient LPE E94T and the end-use product LPE-94 10% Aqueous adequately satisfies the food and non-food use requirements set forth in 40 CFR 158.690 (c) for biochemical pesticides. The overall toxicological risk from human exposure to LPE is negligible.

1. Toxicology Assessment

Adequate mammalian toxicology data are available and support registration of the product containing the active ingredient LPE.

a. Acute Toxicity

The registrant submitted acceptable acute toxicity studies. Based on a lack of mortality observed in albino rats, the oral LD_{50} of both the technical grade LPE E94T and the liquid end-use product LPE-94 10% Aqueous were >5,000 mg/kg, placing them in Toxicity Category IV. Based on a lack of mortality observed in albino rabbits dermally dosed with 2,000 mg/kg of both the technical and the end-use liquid product, the LD_{50} was >2,000 mg/kg, placing them in Toxicity Category III. All animals lived and gained weight after inhaling the product for 4 hours. The LC_{50} for LPE E94T is >2.50, while for the end-use product it is >4.63 mg/L; placing them in Toxicity Category IV.

With a dose of 0.1 ml of liquid LPE-94 10% Aqueous only, one rabbit demonstrated conjunctivitis at the first reading which cleared by 24 hours. This classifies LPE-94 10% Aqueous as practically non-irritating with a Toxicity Category IV. However, when the TGAI was used as a test material, all rabbits had iritis and conjunctivitis one hour after instillation of LPE; all symptoms cleared by 48-hours post-instillation. Based on the data, LPE Technical was considered a minimal irritant and classified as Toxicity Category III. Dermal application of 0.5 g of liquid product did not cause any dermal irritation symptoms up to 72 hours postdosing, placing it in Toxicity Category IV. Based on the data submitted for dermal sensitization, both

the technical and the end-use product are definite contact sensitizers in guinea pigs by the Maximization method. Agency reviews are available in the docket (Refs. 1 and 2)

b. Genotoxicity, Immune Response, Mutagenicity, Developmental, Oncogenicity, Subchronic and Chronic Toxicity

These studies are required, or conditionally required, for all food use biochemical pesticides, however, the registrant submitted published information to justify waivers for these studies (Refs. 3 and 4), based on its presence in all cellular organisms. LPE is present in all cells in all organisms as part of the cell membrane metabolites, from 1-10% depending on cell type. It is also present in high quantities in food products containing egg yolk and meat as well as in human breast milk (Ref. 5). Because of the ubiquitous nature of LPE and non-toxicity of the acute studies, further studies are waived (Refs. 1 and 6).

Data Waivers (Ref. 3) were requested for the following studies:

Studies to detect genotoxicity (OPPTS 870.5300)
Immune Response (OPPTS 880.3800
Mammalian mutagenicity test (OPPTS 870.5195
90-Day feeding (1 species) (OPPTS 870.3100)
90-Day dermal (1 species) (OPPTS 870.3250)
90-Day inhalation (1 species) (OPPTS 870.3465)
Teratogenicity (1 species) (OPPTS 870.3700)
Chronic exposure (OPPTS 870.4100) (Tier III)
Oncogencity (OPPTS 870.4200) (Tier III)

Much of these data regarding LPE and related phospholipids were submitted in support of similar waivers for additional acute toxicity testing, subchronic toxicity testing, and chronic toxicity testing in conjunction with a temporary tolerance exemption (see 40 CFR §180.1199)(Ref. 4) for the use of this active ingredient under an Experimental Use Permit (EPA Reg. No. 70515-EUP-1). The registrant's rationale to support the waivers is that LPE is ubiquitous in nature, and this and related phospholipids are synthesized by microorganisms, plants, and animals. These compounds are also ubiquitous in the human diet. Also, phospholipids have specific roles in cellular functions and in maintaining the integrity of cell membranes. See also memo from Russell Jones, Ph.D. to Sheila Moats, Ph.D., 8 Oct. 1997 (Ref. 6). The aforementioned data may be bridged to support the current waiver requests. In addition, there is a long history of consumption by humans of lipids in food and the Agency known of no instance where lipids have been associated with any toxic effects related to the consumption of food. Due to this knowledge of LPE's presence and function in the human system (Ref. 5) and

the recent acute testing, EPA believes LPE is unlikely to be carcinogenic or have other long-term toxic effects.

Mammalian toxicity data for LPE are summarized in Table 2.

Table 2. Toxicity data requirements

GUIDELINE NO.	STUDY	RESULTS	MRID NO.
152-10, 870.1100	Acute oral toxicity in rats	Both TGAI and EU: LD_{50} is > 5000 mg/kg Toxicity Category IV	452740-01 452736-01
152-11, 870.1200	Acute dermal toxicity in rabbits	Both TGAI and EU: LC_{50} is >2000 mg/Kg Toxicity Category III	452740-02 454361-01
152-12, 870.1300	Acute inhalation toxicity in rats	TGAI LC_{50} is >2.50 mg/L, EU LC_{50} is >4.63; Both TGAI and EU: Toxicity Category IV	452740-05 452736-04
152-13, 870.2400	Primary eye irritation in rabbits	TGAI: Toxicity Category III EU: Toxicity Category IV	452740-04 452736-03
152-14, 870.2500	Primary dermal irritation in rabbits	Both TGAI and EU: Toxicity Category IV	452740-03 452736-02
152-15, 870.2600	Dermal sensitization in guinea pigs	Both TGAI and EU are considered to be contact sensitizers in guinea pigs by the Maximization method.	454357-01 452736-05
152-17, 870.5300	Studies to detect genotoxicity	Waived	N/A
152-18, 870.8700	Cellular immune response	Waived	N/A

GUIDELINE NO.	STUDY	RESULTS	MRID NO.
152-19, 870.5195	Mammalian mutagenicity test	Waived	N/A
152-20, 870.3100	90-day feeding study	Waived	N/A
152-21, 870.3200	90-day dermal study	Waived	N/A
152-22, 870.3250	90-day inhalation study	Waived	N/A
152-23, 870.3700	Developmental toxicity	Waived	N/A
83-1, 870.4100	Chronic exposure	Waived	N/A
83-2, 870.4200	Oncogenicity	Waived	N/A

c. Effects on the Endocrine Systems

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide 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 scientific basis for including, as part of the program, the androgen- and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

Based on the weight of the evidence of available data, no endocrine system-related effects have been identified for LPE and none are expected since LPE is a natural constituent of mammalian cell membranes..

2. Dose Response Assessment

No toxicological endpoints are identified.

3. Aggregate Exposure and Risk Characterization

a. Dietary

i. Food

In the absence of any toxicological endpoints, risk from the consumption of residues is not expected for the general population including infants and children. Sprayed LPE on food crops is relatively low (examples from 0.06-0.18% over native content [Ref. 7]) and are reduced further by catabolism through the lipid metabolic system found in most organisms (Ref.5). Further, commercial phospholipid products containing LPE are in use already and approved by FDA for food use, animal feed and for dietetics (Ref. 5).

ii. Drinking Water

Treatment of crops in the fields may include run-off to surface and ground water, but the compound is a natural metabolite further metabolized by microbial organisms (Ref. 5). Significant exposure to LPE in drinking water is not expected.

b. Other Non-occupational Exposure

LPE is a naturally occurring lipid metabolite and exposure is expected to be universal. In addition, FDA has approved LPE-containing substances for use for many other purposes (Ref. 5).

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

Significant additional human exposure to LPE is not expected in residential, school and day care areas. Commercial phospholipid products containing LPE have been approved by FDA for pharmaceuticals and cosmetic uses (Ref. 5).

a. Occupational Exposure

Agricultural use of LPE is subject to the Worker Protection Standards (WPS), requiring Personal Protective Equipment (PPE), a long-sleeved shirt, long pants, socks, shoes and gloves, plus a 4 hour Restricted Entry Interval (REI).

b. Residential, School and Day Care Exposure and Risk Characterization

In the absence of any toxicological endpoints, risk from the consumption of residues is not expected for populations in residential, school and day care including infants and children.

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

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. Margins of exposure (safety) are often referred to as uncertainty (safety) factors. In this instance, based on all the available information, the Agency concludes that LPE is practically non-toxic to mammals, including infants and children. Thus, there are no threshold effects of concern and, as a result the provision requiring an additional margin of safety does not apply. Further, the provisions of consumption patterns, special susceptibility, and cumulative effects do not apply. LPE is found naturally in many foods already consumed by infants and children, human breast milk, eggs, any kind of organic food. And, as no toxic endpoints have been identified, any hazard is impossible to determine. As a result, EPA has not used a margin of exposure (safety) approach to assess the safety of LPE.

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

Aggregate exposure to LPE by field workers and applicators may occur via oral, dermal and inhalation routes. These risks are measured via the acute toxicity studies submitted to support registration. The oral toxicity studies for LPE showed no toxicity (Toxicity Category IV), the risks anticipated from oral exposure are considered minimal. Because the inhalation toxicity studies for LPE showed no toxicity (Toxicity Category IV), the risks anticipated for this route of exposure are also considered minimal.

Results of the acute dermal toxicity study indicated no toxicity at the maximum dose tested (2,000 mg) (Toxicity Category III) and no significant dermal irritation (Toxicity Category IV). Based on these results, the anticipated risks from dermal exposure are also considered minimal.

Therefore, the risks from aggregate exposure via oral, dermal and inhalation exposure are a compilation of three low risk exposure scenarios and are negligible.

Dermal sensitization may occur, as the products are sensitizers. However, this risk is mitigated as long as the product is used according to label directions, which requires the use of protective equipment (a long-sleeved shirt and long pants, socks, shoes and gloves) by users and a 4-hour restricted re-entry interval into treated areas. Aggregate exposure to LPE by the consumer would include other sources in addition to the limited amount on the agricultural products. Commercial phospholipid products containing LPE are used in the technical industry, and have been approved by FDA for food use, pharmaceuticals, cosmetics and dietetics and animal feed (Ref. 5).

7. Cumulative Effects

LPE is not toxic and it is not anticipated there would be cumulative effects from common mechanisms of toxicity.

8. Risk Characterization

The Agency has considered LPE in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U. S. population in general, and to infants and children in particular, will result from the use of LPE-94 10% Aqueous when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Effects Hazard Assessment

The end use product LPE-94 10% Aqueous is intended for agricultural and horticultural use. When applied according to the proposed label directions, no direct exposure of birds or aquatic organisms to LPE-94 10% Aqueous is expected to occur. Moreover, the active ingredient is a natural metabolite of a common biological lipid. Many published studies were supplied to the Agency which indicate that LPE-94 10% Aqueous's potential environmental/ecological effects (Ref. 8) are likely to be negligible. As a result, organism/ecological effects studies were waived for these particular uses of LPE-94 10% Aqueous. However, standard precautionary label statements under "Environmental Hazards" are presented on the label.

2. Environmental Fate and Ground Water Data

The need for environmental fate and groundwater data (Tier II, (40 CFR Section 158.690(d)(2)(vii through xv)) was not triggered because the Tier I studies were waived. Risk is minimal due to the lack of exposure, low toxicity, use pattern, and application methods.

3. Ecological Exposure and Risk Characterization

Sprayed LPE residues are low (examples are from 0.06-0.18% over native content [Ref. 7]), and are reduced further by catabolism through the lipid metabolic system found in most organisms (Ref. 5). Minimal potential for exposure exists to insects, fish and other nontarget wildlife as a result of LPE-94 10% Aqueous use.

D. EFFICACY DATA

No efficacy data are required, because no public health uses are involved.

IV. Risk Management Decision

A. DETERMINATION OF ELIGIBILITY FOR REGISTRATION

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

To satisfy criteria “A” above, LPE is not expected to cause unreasonable adverse effects when used according to label instructions. Criteria “B” is satisfied by the current label and by the data presented in this document. It is believed that this new pesticidal active ingredient will not cause any unreasonable adverse effects, will enhance fruit, hasten ripening and increase shelf life, satisfying Criteria “C”. Criteria “D” is satisfied by the data submitted and the low exposure to the product when used according to the label's directions.

Therefore, LPE is eligible for registration. The uses are listed in Table 4, Appendix A.

B. REGULATORY POSITION

1. Unconditional Registration

All data requirements have been fulfilled and/or waived by the Agency and the Biopesticides and Pollution Prevention Division recommends unconditional registration of products which contain LPE as their sole active ingredient.

2. Tolerances for food uses and/or exemptions

EPA received a pesticide petition (1F6244) from JP BioRegulators, Inc., proposing [pursuant to section 408(b)(2)(D) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. section 346], to amend 40 CFR Part 180 by establishing an exemption from the requirement of a tolerance for the biochemical pesticide, lysophosphatidylethanolamine.

2. CODEX Harmonization

There are no CODEX values for LPE.

3. Nonfood Re/Registrations

There are no non-food issues at this time. The non-food uses are listed in Appendix A, Table 4.

4. Risk Mitigation

There are no significant risk issues. Risks to workers are mitigated by protective clothing requirements and a 4-hour re-entry interval restriction.

5. Endangered Species Statement

Given the specificity of this biochemical pesticide and based on the intended use pattern., and the results of toxicity and exposure data from the public scientific literature and from the data submitted by the applicant, the Agency has determined that this action will have no effect on currently listed endangered and threatened species.

C. LABELING RATIONALE

It is the Agency's position that the labeling of LPE-94 10% Aqueous and the technical grade active ingredient LPE E94T containing, respectively, 10% and 94% LPE complies with current pesticide labeling requirements.

1. Human Health Hazard

a. Worker Protection Standard

This product comes under the provisions of the Worker Protection Standards (WPS). PPE (long-sleeved shirt and long pants, socks, shoes, and gloves) and REI (4-hour) required.

b. Non-Worker Protection Standard

There are no non-WPS human health hazard issues.

c. Precautionary Labeling

The Agency has examined the toxicological data base for LPE E94T and LPE-94 10% Aqueous product and concluded proposed precautionary labeling (i.e. Signal Word, Statement of Practical Treatment and other label statements) adequately mitigates any risks associated with the proposed uses.

Technical product Precautionary Labeling: For LPE E94T – "Caution"

Hazards to Humans and Domestic Animals:

Harmful if absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wear protective eyewear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Wear long-sleeved shirt and long pants, socks, shoes, and gloves. Remove and wash contaminated clothing before reuse.

Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

End-Use product Precautionary Labeling: For LPE-94 10% Aqueous – "CAUTION."

Hazards to Humans and Domestic Animals:

Harmful if absorbed through skin. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse. Wear: Long-sleeved shirt and long pants, socks, shoes, and gloves.

Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

2. Environmental Hazards Labeling

End-Use Product Environmental Hazards Labeling: Although LPE is considered non-toxic to the environment, the environmental hazard statement is nevertheless required on the end-use product's label.

3. Application Rate

It is the Agency's position that the labeling for the pesticide product containing LPE complies with current pesticide labeling requirements. The Agency has not stipulated a maximum number of applications for the active ingredient. Pre-harvest applications should use conventional spray or foliar application equipment at a rate of 100-400 ppm depending on crop. Mix LPE with water at a rate of 1 gallon per 100 gallons of water. Begin applications at 30 to 20 days before harvest and continue at 7 to 10 day intervals. Post-harvest dips or sprays are applied immediately after harvest, before storage, at a rate of 25-100 ppm LPE, while use as a solution for maintenance of cut flowers is at the same rate.

D. LABELING

(1) Product name: **LPE E94T**

Active Ingredient:
Lysophosphatidylethanolamine (LPE). 94.0%
Other Ingredients 6.0%

Total 100.00%

(2) Product name: **LPE-94 10% Aqueous**

Active Ingredient:
Lysophosphatidylethanolamine 10.0%
Other Ingredients 90.0%

Total 100.00%

Signal word is "CAUTION". Dermal toxicity and hypersensitivity warning is appropriate.

The product shall contain the following information:
- Product Name
- Ingredient Statement
- Registration Number
- Signal Word (CAUTION)

V. Actions Required by Registrants

There are no data requirements, label changes or other responses necessary for the reregistration of the end-use product since the product is being registered after November 1984 and is, therefore, not subject to reregistration. Both the technical grade product and the end product were registered March 26, 2002. There are no existing stocks provisions at this time.

VI. Appendix A

Table 4 lists the use sites for the product. The labels for the product are also attached.

Table 4. Field Crop, Cut Flowers, Use Site Registration/Reregistration

LPE-94 10% Aqueous Use Sites: Field Crops, Storage Facilities, Horticultural Facilities	Official date registered: March 26, 2002

VII. References

1. USEPA; Science Review in Support of Registration of LPE E94T Technical and LPE 94 20% Aqueous Growth Regulator, memo from Jones, Russell S., Ph.D., to Carol E. Frazer, Ph.D., 13 Sep. 2001.

2. USEPA; Data Evaluation Record: Skin Sensitization (MRID 454357-01), memo from Reilly, Sheryl K., Ph.D., to Carol E. Frazer, Ph.D., 21 Jan. 2002.

3. JP BioRegulators, Inc.: Waiver Request from Biochemical Pesticides Toxicology Data Requirements, 2000.

4. Palta, Jiwan, Dr. and Hartman, Christina L., Dr.: Phospholipid Safety Data in Support of a Petition Proposing a Temporary Exemption from the Requirement of a Tolerance for Phospholipid for Use in Grapes, Tomatoes, Apples, Pear, Peaches, Nectarines, Citrus, Cranberries and Strawberries, 1997 (MRID 443399-05).

5. JP BioRegulators, Inc.: A Review on Lysophosphatidylethanolamine and Related Phospholipids, 2000.

6. USEPA. An Experimental Use Permit (EUP) and Petition for a Temporary Tolerance Exemption for Phospholipid; memo from Jones, Russell S., Ph.D., to Sheila Moats, Ph.D., 8 October 1997.

7. Nutra-Park, Inc., 2002: Effect of LPE Applications; Memo to Carol E. Frazer, Ph.D.

8. Palta, Jiwan, Dr. and Hartman, Christina L., Dr.: Phospholipid – Safety Data for Environmental Effects, 1997 (MRID 443399-06).6