# US Environmental Protection Agency
# Office of Pesticide Programs

## BIOPESTICIDES REGISTRATION ACTION DOCUMENT

**2,6-Diisopropylnaphthalene**

**(PC Code 055803)**

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

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# I. EXECUTIVE SUMMARY

## A. IDENTITY

The Technical Grade Active Ingredient (TGAI) 2, 6-Diisopropylnaphthalene ( referred to as 2, 6-DIPN), is an oderless crystalline solid. 2,6-DIPN has a non-toxic mode of action. While it does not occur naturally, 2,6-DIPN is functionally and structurally identical to the naturally occurring plant growth regulator in potatoes. The end-use product Amplify® Sprout Inhibitor, that contains 99.7% of 2,6-DIPN, is manufactured by an integrated process. The product chemistry data submitted by the applicant satisfies the requirements for product identity.

## B. USE / USAGE

The end-use product Amplify® Sprout Inhibitor is to be used as a plant growth regulator to suppress sprouting of stored potatoes. It will be applied using conventional fogging systems to form aerosols for direct treatment of stored potatoes.

## C. RISK ASSESSMENT

### 1. Human Health Risk Assessment

Data submitted were evaluated under the provisions of the Food Quality Protection Act of 1996. Acute mammalian toxicology data support the low toxicity profile of the product. These data are sufficient to support a temporary tolerance for residue of 2, 6-DIPN.

The test substance, 2,6-DIPN was classified as Toxicity Category IV based on the Acute Oral Toxicity Study, the Acute Dermal Toxicity Study, the Acute Inhalation Toxicity Study and the Primary Eye and Skin Irritation Studies. A Dermal Sensitization Study found that 2,6-DIP is not considered to be a contact sensitizer. During the development of 2,6-DIPN, no incidents of hypersensitive reactions were observed or reported. Personnel have used this product under an experimental use permit in testing facilities, commercial storage warehouses, and in manufacturing operations without any observed incidents.

Four short-term genotoxicity assays were submitted and reviewed. A bacterial reverse mutation assay (Ames test), an *in vivo* / *in vitro* unscheduled DNA synthesis in rat primary hepatocytes at two time points, and an *in vivo* mouse micronucleus assay were conducted with 2,6-DIPN and were negative. A mouse lymphoma study conducted with 2,6-DIPN was weakly positive in the absence of metabolic activation and equivocal in the presence of metabolic activation, in both cases at concentrations that showed marked cytotoxicity. Based on a weight of evidence evaluation of mutagenicity data for 2,6-DIPN, there is no concern for genotoxicity of 2,6-DIPN.

A 90-day rat feeding study of 2,6-DIPN was conducted at levels of 750, 1,500 and 3,000 ppm (0, 53.9, 104, and 208 mg/kg/day for males and 0, 61.8, 121, and 245 mg/kg/day for females). Based on microscopic findings at 3,000 ppm, the no-observable-adverse-effect level (NOAEL) is 1,500 ppm.

A prenatal development toxicity study of 2,6-DIPN in rats was conducted at doses of 0, 50, 150, and 500 mg/kg/day. The NOAEL for maternal toxicity was considered to be 50 mg/kg/day based on decreased body

weight and feed consumption and the NOAEL for prenatal development toxicity was considered to be 150 mg/kg/day based on decreased fetal body weight and a possible treatment related cartilage anomaly.

Tier III tests involving chronic testing and oncogenicity testing were not required.

EPA has considered 2,6-DIPN in light of the relevant safety factors in the Food Quality Protection Act (FQPA) of 1996 and under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended. EPA has determined that there is a reasonable certainty of no harm to human adults, infants and children exposed to the product from all anticipated dietary and other exposures evaluated with the current database.

**2. Ecological Risk Assessment**

EPA has concluded that it does not anticipate any avian, freshwater fish and aquatic invertebrates, beneficial insects and honeybees or nontarget plant toxicity to be caused by the proposed use of the product, which is limited to indoor uses in commercial potato warehouses.

## D. ADDITIONAL DATA REQUIREMENTS/LABEL RESTRICTIONS

No requirements are listed at this time.

## II. OVERVIEW

### A. ACTIVE INGREDIENT AND PRODUCT OVERVIEW

**Common Names:** 2,6-Diisopropylnaphthalene (2,6-DIPN)

**Chemical Name:** 2,6-Diisopropylnaphthalene

**Chemical Formula:** $C_{16}H_{26}$

**Chemical Family:** Substituted Naphthalene

**Molecular Weight:** 218

**Trade and Other Names:** Amplify® Sprout Inhibitor

**OPP Chemical Code:** 055803

**CAS Registry Number:** 24157-81-1

**Basic Manufacturer:** Platte Chemical Co.
7251 4th Street., P.O. Box 667
Greeley, CO 80632-0667

### B. USE PROFILE

The following is information on the proposed uses with an overview of use sites and application methods.

**Type of Pesticide:** Biological Plant Growth Regulator

**Use Sites:** For use in potato storage warehouses.

**Plant Growth Regulator Effect:** Sprout suppression.

**Formulation Type:** Solid material.

**Method and Rates of Application:** The product is applied directly to a conventional aerosol fogging unit, which then produces an aerosol that is applied directly to stored potatoes via air duct systems. The application rate is a single application of 16.6 ppm or 1.0 lb. Active ingredient per 600 cwt. (60,000 lb.) of potatoes.

**Use Practice Limitations:** Amplify® Sprout Inhibitor is to be applied only on stored potatoes.

**Timing:** Amplify® Sprout Inhibitor is applied prior to the end of the natural dormancy period of the potato and before sprouting occurs. One application is made and potatoes are held for 30 days after application before being released into commercial commerce.

## C. ESTIMATED USAGE

Estimates based on existing commercial use cannot be made since this is the first conditional registration of this active ingredient. The biochemical pesticide has been used in an experimental use permit (EUP# 34704-EUP-13) from September 28, 1999 to 9/28/2000. Usage of the end-use product (EP) during the experimental period was projected to be 5000 pounds 2, 6-DIPN on 300 millions pounds of stored potatoes over the permitted research period.

## D. DATA REQUIREMENTS

The submissions comply with Agency data requirements for granting this conditional registration under Sect 3(c)(7)(C) of the Federal Insecticide, Fungicide and Rodenticide Act and have been reviewed by the Biopesticides and Pollution Prevention Division. For 2,6-DIPN, the product identity, manufacturing batch analysis, as well as the data/information submitted for acute mammalian toxicology and ecological effects are sufficient to allow the proposed use patterns. Based on evaluations of the submitted data and information as discussed in this document, the Agency foresees no unreasonable adverse effects to human health and the environment form the use of 2,6-DIPN, as long as it is used as labeled.

Conditions of registration for this new active ingredient include the submission of:

(i) Livestock feeding studies
(ii) Enforcement analytical methods for livestock and potatoes

While the submission of these studies are a condition of the registration, the Agency believes that its analyses, which rely on the available data, supplemented with conservative assumptions, are sufficient to support a tolerance for the short period during which these studies will be conducted.

## E. REGULATORY HISTORY

### 1. Experimental Use Permits (EUP) and Temporary Tolerance:

On July, 1998, Platte chemical Company submitted an EUP application and a petition for a temporary tolerance exemption (PP8G5008) for the use of 2, 6-DIPN on stored potatoes. A temporary tolerance exemption was established on September 22, 1999 , (64 FR 51245); and subsequently, the EUP was approved for use of 5000 pounds 2, 6-DIPN on 300 millions pounds of stored potatoes starting September 28, 1999. The application took place in storage facilities located in Minnesota, Idaho, Maine, North Dakota, Oregon, Washington and Wisconsin. The EUP expired on September 28, 2000.
On June 26, 2000, Platte Chemical, Co., requested an extension of the EUP. A notice of filling for the tolerance exemption petition (PP 8G5008) was published on August 30, 2000 (65 FR 52740). However, the applicant decided to withdraw the EUP application and petition, and submitted a section3 application for the registration of the product Sprout Inhibitor.

### 2. Section 3 Registration

On June 21, 2001, the Agency received an application from Platte Chemical Company to register Amplify® Sprout Inhibitor containing 97% of 2, 6-DIPN, as a potato sprout inhibitor. A notice of receipt of the application for registration of 2, 6-DIPN as a new active ingredient was published in the Federal

Register on September 19, 2001 (66 FR 48254), with a 30-day comment period. No comments were received as a result of this publication. EPA issued a notice pursuant to section 408(d)(3) of the FFDCA (21 USC 346a(d)(3)), announcing the filing of a pesticide tolerance petition (PP 1F6338) by Platte Chemical Company, requesting an exemption from the requirement of a tolerance for residues of 2, 6-DIPN (66 FR 48677). Comments were received in response to this FR Notice and are discussed and addressed in the final rule **(68 FR 47246)**

## F. CLASSIFICATION

2,6-DIPN has a non-toxic mode of action involving sprout inhibition of potatoes. Although it is not necessarily naturally occurring, it is functionally identical and essentially similar to a registered naturally-occurring plant growth regulator and is functionally identical to a registered product.

## G. FOOD CLEARANCES/TOLERANCES

The Agency evaluated data under the Food Quality Protection Act (FQPA) of 1996. Safety factors were considered for human health effects, as well as aggregate and cumulative exposures. Dietary exposure and risk from eating food treated with the pesticide is expected to be minimal to non-existent. Based on the data submitted a temporary tolerance of 3 ppm on potato peel was established for residues of 2, 6-DIPN when used in/on potatoes, on **August 8, 2003** , **(68 FR 47246)**. **This tolerance will expire on May 31$^{th}$, 2006**.

## III. SCIENCE ASSESSMENT

### A. Physical and Chemical Properties Assessment

The product chemistry data requirements for 2,6-Diisopropylnaphthalene (2,6-DIPN) have been satisfied. Data submitted are summarized in Table 1.

### 1. Product Identity and Mode of Action

*Product Identity:* 2,6-Diisopropylnaphthalene is a synthetic plant growth regulator which the Agency has classified as a biochemical pesticide. 2,6-DIPN has a non-toxic mode of action. While it does not occur naturally, it is functionally identical to the naturally occurring plant growth regulatory in potatoes.
*Mode of Action:* The product 2,6-DIPN is a plant growth regulator that, when applied to stored potatoes, will suppress sprouting.

### 2. Food Clearances/Tolerances

An temporary tolerance for residues of 2,6-DIPN on potatoes **of 0.5 ppm (whole potatoes) and 3ppm (potato peels)** has been proposed and will be published in the Federal Register on approval of this registration action. There is no Codex Maximum Residue Level (MRL) for 2,6-DIPN.

### 3. Physical And Chemical Properties Assessment

The product manufacturing process, batch analysis, and physical and chemical properties data, support the conditional registration of 2,6-DIPN (Table 1). However, as a condition of the registration, an enforcement analytical method for livestock and potatoes must be submitted.

**Table 1: Product Chemistry / Physical and Chemical Properties of 2,6-Diisopropylnaphthalene**

| OPPTS Guideline Number | OPPTS Guideline Name | Results | MRID No. |
|---|---|---|---|
| 880.1100 | Product Identity and Composition | Acceptable | 44614102 |
| 880.1200 | Description of Methods Used to Manufacture the Product | Acceptable | 44614101 |
| 880.1400 | Discussion of the Formation of Impurities | Acceptable | 44614101 |
| 830.1700 | Analysis of Samples | Acceptable | 44614102 |
| 830.1750 | Certified Limits | Acceptable | 44614102 |
| 830.1800 | Enforcement Analytical Method | Acceptable * w/conditions. An additional enforcement analytical method on livestock & potatoes must be submitted. | 44614102 |
| 830.6302 | Color | N 9.5 | 44614103 |
| 830.6303 | Physical state | Crystalline solid | 44614103 |
| 830.6304 | Odor | Odorless | 44614103 |

| | | | |
|---|---|---|---|
| 830.6313 | Stability to normal and elevated temperatures, metals and metal ions | Stable under normal temperatures and pressures; and under ordinary conditions of use. Stable with Al and Zn metal. Stable when exposed to UV light. | 44614103 |
| 830.6314 | Oxidation/reduction: Chemical incompatibility | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.6315 | Flammability | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.6316 | Explodability | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.6317 | Storage stability | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.6319 | Miscibility | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.6320 | Corrosion characteristics | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.6321 | Dielectric breakdown voltage | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.7000 | pH | 6.00 | 44614103 |
| 830.7050 | UV/visible absorption | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.7100 | Viscosity | Not applicable - product is a solid. | N/A |
| 830.7200 | Melting point/melting range | 67.3°C - 68.9°C | 44614103 |
| 830.7220 | Boiling point/boiling range | Not applicable - product is a solid. | N/A |
| 830.7300 | Density/relative density/bulk density | 0.49 g/ml at 25°C | 44614103 |
| 830.7370 | Dissociation constant | Not applicable. Not a requirement for Subdivision M. | N/A |
| 830.7520 | Particle Size | Not applicable for TGAI (40 CFR 158.190) | N/A |
| 830.7550 | Partition coefficient (*n*-octanol/water): | Measurement not taken due to the extremely low water solubility of 20 ppb. | N/A |
| 830.7840 | Water solubility: | Measurement not taken due to the extremely low water solubility of 20 ppb. | N/A |
| 830.7950 | Vapor pressure | $6.1 \times 10^{-10}$ 25°C | 44614103 |

## B. HUMAN HEALTH ASSESSMENT

### 1. Food Clearances/Tolerances

This is the first proposed section 3(c)(7)(C) conditional registration of the active ingredient 2,6-DIPN. It has been used in the field under EUP # 34704-EUP-13, during which time a temporary exemption from the requirement of a food tolerance was established. Allowable residues under the proposed temporary tolerance are 0.5ppm in or on whole potatoes and 3ppm in or on potato peels **(68 FR 47246) August 08, 2003)**.

There is a reasonable certainty that no harm is likely from exposure to 2,6-DIPN. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. Below is the toxicology assessment, and discussion of other factors under the Food Quality Protection Act (1996), which led to the decision regarding the temporary tolerance for residues of 2,6-DIPN to be granted concomitant with the conditional registration of the pesticide (40 CFR 180.1208).

## 2. Toxicology Assessment

Mammalian toxicology studies have been submitted and are sufficient to support the conditional registration of 2,6-DIPN for the proposed use pattern. Summaries of the acute toxicological studies (Table 2) are discussed below.

**Table 2. Acute Mammalian Toxicity: Tier I**

| OPPTS Guideline Number | OPPTS Guideline Name | Toxicity Category | Results | MRID No. |
|---|---|---|---|---|
| 870.1100 | Acute Oral Toxicity - Rat | IV | The single dose Oral $LD_{50}$ is greater than 5000 mg/kg of body weight. | 44614104 |
| 870.1200 | Acute Dermal Toxicity - Rabbit | IV | The single dose Dermal $LD_{50}$ is greater than 5000 mg/kg of body weight. | 44614105 |
| 870.1300 | Acute Inhalation Toxicity - Rat | IV | The single dose exposure Acute Inhalation $LC_{50}$ is greater than 2.60 mg/L. | 44614106 |
| 870.2400 | Primary Eye Irritation - Rabbit | | Practically non-irritating to the eye. | 44614107 |

| | | | | |
|---|---|---|---|---|
| 870.2500 | Primary Dermal Irritation - Rabbit | | Slightly irritating to the skin. Primary dermal index based on 1-72 hours was 0.3. | 44614108 |
| 870.2600 | Dermal Sensitization - Guinea Pig | | Not considered a contact sensitizer. | 44614109 |

The classification of 2,6-DIPN as a biopesticide was based on its structural and functional similarity to 1-isopropyl-4,6-dimethylnaphthalene, 1-methyl-7-isopropylnaphthalene, and 4-isopropyl-1,6-dimethylnaphthalene which are naturally occurring plant growth regulators found in plant tissues. In addition, 2,6-DIPN is a sprout inhibitor, with a non-toxic mode of action. Therefore, the toxicity data reviewed include acute oral, dermal and inhalation toxicity studies, eye and skin irritation studies, a dermal sensitization study, subchronic feeding and developmental toxicity studies and genetic toxicity studies.

2,6-DIPN is classified in toxicity category IV for mammalian acute oral toxicity ($LD_{50}$ >5000 mg/kg; OPPTS 870.1100; 152-10; MRID 446141-04), acute dermal toxicity ($LD_{50}$ > 5000 mg/kg; OPPTS 870.1200; 152-11; MRID 446141-05), and acute inhalation toxicity ($LC_{50}$ >2.60 mg/L; OPPTS 870.1300; 152-12; MRID 446141-06), eye irritation (OPPTS 870.2400; 152-13; MRID 446141-07) and dermal irritant (OPPTS 870.2500; 152-14; MRID 446141-08). The active ingredient was not allergenic on skin (not a dermal sensitizer; OPPTS 870.2600; 152-15; MRID 446141-09).

The subchronic toxicity study in rats (OPPTS870.3100; 152-20; MRID 450493-01) suggests a no-observed-effect level (NOEL) of 104 mg/kg/day (104 or 121 mg/kg/day for males and females, respectively). The lowest-observed-e-adverse-effect level (LOAEL) is 208 mg/kg/day (208 and 245 mg/kg/day for males and females, respectively), based on minimal decreases in body weight gains, food consumption, adrenal effects (including increased absolute and relative organ weights and adrenal cortical hypertrophy) and kidney toxicity (evidence of tubular nephrosis in male rats).

In the rat developmental toxicity study (OPPTS 870.3700, 152-23; MRID 450001-01), the maternal toxicity LOAEL is 150 mg/kg/day based on reduced body weight gains and food consumption. The maternal toxicity NOAEL is 50 mg/kg/day. The developmental toxicity LOAEL is 500 mg/kg/day based on reduced fetal body weights and a slightly increased incidence of a skeletal alteration (fusion of cartilaginous bands in the cervical centra). The developmental toxicity NOAEL is 150 mg/kg/day.

A mouse lymphoma gene mutation assay (OPPTS 870.5300; 152-17; MRID 454388-01) showed that 2, 6-DIPN might be mutagenic without metabolic activation at doses between 10-30 µg /mL. With metabolic activation, the results were equivocal at doses between 25-90 µg /mL. Cytotoxicity was observed in tests using the aforementioned doses, with and without metabolic activation. No genotoxicity was observed in other acceptable studies including a reverse mutation (Ames) assay (OPPTS 870.5100; 152-17; MRID 446141-11), *in vivo/in vitro* unscheduled DNA synthesis (UDS) assays in rat primary hepatocytes (OPPTS 870.5550; 152-17; MRID 446141-10), and a mouse micronucleus assay (OPPTS 870.5395; 152-17; MRID

446141-12). The collective data from the four-study mutagenicity battery demonstrates that 2, 6-DIPN is not likely to be mutagenic.

**a. Toxicological Endpoints**

1. *Acute toxicity*: The Acute toxicity studies were acceptable in accordance with the guidelines as discussed in III. A above All studies were performed at a single limit dose with no observable (non-lethal)toxic endpoints.

2. *Short- and intermediate-term toxicity*: Although the rat developmental toxicity study indicates a lower maternal NOEL (50mg/kg/day) for similar toxicity than the subchronic toxicity study (reduced body weight, weight gain and food consumption), the maternal LOAEL of 150 mg/kg/day falls between the subchronic NOEL of 104-121 mg/kg/day and the subchronic LOAEL of 208-245 mg/kg/day. The maternal NOEL of 50 mg/kg/day from the developmental toxicity study may be appropriate for use in characterization of risks for the subpopulation of women 13-49 years of (child-bearing) age. However, the 104 mg/kg/day NOEL in the subchronic study was selected as the endpoint for short- and intermediate-term dietary assessments since the effects observed at the subchronic LOAEL (208-245mg/kg/day) were more thoroughly defined than the developmental effects observed at the LOAEL (500mg/kg/day) in the developmental toxicity study, which were minimal.

A reference dose (RfD) of 1 mg/kg/day is established by dividing the 104 mg/kg/day NOEL by a 100-fold uncertainty factor (10X for interspecies extrapolation and 10X for intraspecies variability). An extra 10-fold uncertainty factor for the absence of chronic toxicity data were not applied because 2,6-DIPN has been classified as a biochemical pesticide and chronic studies are not required to support registration (40 CFR 158.690(c). Available developmental toxicity data on 2,6-DIPN does not indicate extra sensitivity of offspring when compared with that of adult animals, but a developmental toxicity study in a second species and a multigeneration reproduction toxicity study are needed to fully determine age-related differences in response. In addition, residues have been detected in treated potatoes under laboratory and field conditions. Therefore, the default safety factor of 10X is retained., and acute and chronic population adjusted doses (aPAD and cPAD) for dietary risk characterizations are established by dividing the RfD by 10X (accounting for age-related sensitivity for the subpopulations of infants and children). Therefore, the aPAD and cPAD are 0.1 mg/kg/day.

**b**. **Chronic Toxicity**:

The registrant was not required to conduct chronic toxicity data under 40 CFR §158.690(c), because no toxicity was observed in the acute and subchronic toxicity studies. Moreover, as discussed above, the subchronic toxicity studies are more relevant to exposure anticipated by the use pattern, were available so the RfD discussed in the previous section was used as the chronic toxicity endpoint.

**c**. **Carcinogenicity**:

Based on the 90-day oral toxicity study and the genotoxicity/mutagencity studies, there were no results to indicate potential neoplastic changes, and the genetic toxicity studies did not suggest carcinogenic potential in mammalian cells.

**3. Exposure Assessment**

**a Dietary Exposure from food and feed uses**:

There is a potential for dietary exposure to 2, 6-DIPN, which can occur following its application to stored potatoes. According to the label, the plant growth regulator is to be applied at a rate of 16.6 ppm (w/w), and as many as three applications can be used in a storage period with a minimum interval between application and use of the treated potatoes of 30 days.

**i. Residue Profile**.

The submitted residue chemistry data for the use of 2, 6-DIPN on potatoes is limited, and important factors in this assessment depend on default assumptions or hypothetical calculations having a low level of confidence.

For purposes of this rule, the regulated residue is considered to be 2, 6-DIPN, and a potential for some accumulation of 2, 6-DIPN residues in body and subcutaneous fat was observed. These results and the possible use of peels with residues from treated potatoes as livestock feed (processed potato wastes are used for this purpose) suggest that residues of 2, 6-DIPN may occur in meat and milk; however, this has not been evaluated in a livestock metabolism study.

Limited field and laboratory residue data suggested tolerance levels as high as 0.5 ppm in/on whole potatoes, 3 ppm on potato peels, 1.35 ppm in meat and meat by-products, and 0.7 ppm in milk.

The analytical method for 2,6-DIPN has a level of quantification (LOQ) of 0.02 ppm and field and laboratory studies suggests that 20 ppm is a likely maximum commercial application rate for 2,6-DIPN. Residue levels expressed as 2,6-DIPN were reported at 3 ppm in potato peels and 0.5 ppm in whole potatoes.

In a published report (MRID 45163201), the investigators noted that DIPNs could accumulate in the fat of treated rats suggesting a potential for secondary residues in meat and milk from livestock fed treated potatoes, but a livestock metabolism study was not submitted. Worst-case estimates of secondary residues were calculated for meat (1.35 ppm) and milk (0.7 ppm) of beef/dairy cattle fed waste from 2,6-DIPN-treated processed potatoes.

Supplementary metabolism information was submitted on 2, 6-DIPN in rats from two published articles (MRID 451632-01). In one study, rats were given either a single dose or 30 daily oral doses, at 100 mg 2, 6-DIPN per kg body weight. Residues of 2, 6- DIPN were detected in all tissues two hours after receiving the test dose. With the exception of body and subcutaneous fat, DIPN was not detected 48 hours after the single (100 mg/kg) dose. Peak levels in body and subcutaneous fat were found 24 hours after dosing at 75

and 85 µg/g of tissue, respectively; these levels declined to approximately 60 µg/g by 48 hours following the single dose. Results were similar in rats given the repeated doses with the peak levels in body and subcutaneous fat reported to be 150 and 90 µg/g, respectively, at two hours following administration of the last dose. By 30 days after this last dose was given, the 2, 6-DIPN levels in fat had declined to 5 µg/g. The estimated half-life for 2, 6-DIPN in fat was approximately 7 days, and the investigators noted that DIPNs had a small potential for accumulation in fat (levels increased from 2 to 7% over those found after a single dose in subcutaneous and body fat, respectively). Worse-case estimates of secondary residues were calculated for meat (1.35ppm) and milk (0.7ppm) of beef/dairy cattle fed waste from 2,6 -DIPN-treated processed potatoes. These tolerance provide a reasonable certainty of no harm and livestock feeding studies will allow further refinement of these estimates.

In the second article, it was noted that 2, 6-DIPN was metabolized in rats primarily by way of an oxidative pathway involving the isopropyl groups. Five metabolites were identified in urine from rats given an oral dose of 240 mg 2, 6-DIPN per kg body weight, and the majority of the DIPN residues recovered in the urine (23% of the dose at 24 hours) was represented by 2-[6(1-hydrosy-1-methyl)ethylnaphthalen-2-yl]-2-hydroxypionic acid (17.5% of the dose). This study did not explain the fate of the remaining 77% of the administered dose. The livestock feeding study should determine the fate of the administered dose, but because worse case estimates were used to establish the tolerances, there is a reasonable certainty of no harm.

Acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software (DEEM™ version 1.30) which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII, 1994-1996/1998).

For acute exposure assessments, individual one-day food consumption data define an exposure distribution which is expressed as a percentage of the acute population adjusted dose (aPAD is 0.1 mg/kg). For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form on the commodity residue list is multiplied by the average daily consumption estimate for the food/food-form. The resulting residue consumption estimate for each food/food-form is summed with the residue consumption estimate for all other food/food-forms on the commodity residue list to arrive at the total estimated exposure. Exposure estimates are expressed as mg/kg body weight/day and as a per cent of the cPAD (0.1 mg/kg/day). It's just as likely that the exposure estimates are appropriate, given that it is not uncommon for the peels to be eaten. These procedures were performed for each population subgroup. As a condition of registration, the registrant will be required to submit livestock feeding studies and enforcement analytical methods for livestock and potatoes; however, EPA believes that its analyses, which rely on the available data, supplemented with conservative assumptions, are sufficient to support a tolerance for the short period during which these studies are conducted.

**ii. Dietary exposure from drinking water**.

Pesticide residues in drinking water are not expected to result from this use. The use is restricted to application in a commercial warehouse to stored potatoes. In addition, the label will restrict users from contaminating water supplies when cleaning equipment or disposing of equipment wash waters.

**iii. From non-dietary exposure**.

The term "residential exposure" is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets).
2,6-DIPN is not registered for use on any sites that would result in residential exposure, but is restricted to use in commercial warehouses.

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

**i. Occupational and Residential Exposure and Risk**

Due to the proposed use pattern in commercial potato warehouses, no residential exposures will occur and negligible occupational exposure may occur. Any potential occupational exposure is mitigated by the required personal protective equipment on the label.

**ii. Residential, School and Day Care Exposure and Risk Characterization**

Due to the proposed use pattern of the product in commercial potato warehouses, no exposures to infants and children in school, residential and day care facilities will occur.

**c. Drinking Water Exposure and Risk Characterization**

Based on the low use rate and an indoor use pattern that is not widespread, residues of 2,6-DIPN in drinking water and exposure from this route is unlikely.

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

Acute exposures for infants and children one to six years of age were estimated at 0.000682 mg/kg bw/day (MOE = 73309). For the most highly exposed population subgroup, children of one to six years of age, chronic exposure was estimated to be 0.000119 mg/kg bw/day or <0.1 percent of the RfD.

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

The Agency has considered the various routes of exposure and potential risks of the product and determined that the proposed use of the active ingredient does not pose significant risk to all populations, including infants and children.

**6. Cumulative Effects**

Section 408(b)(2)(D)(v) of the FFDCA requires the Agency to consider the cumulative effect of exposure to 2,6-DIPN and to other substances that have a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. 2,6-DIPN has a non-toxic mode of action.

Thus, there is no indication nor any evidence to suggest that this biochemical pesticide shares any common mechanisms of toxicity with other substances. Therefore, cumulative exposure concerns are not anticipated

**7. Effects on the Immune and Endocrine Systems**

EPA is required under the FFDCA, 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 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 FEFRA an, 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).There is no information to suggest that 2,6-DIPN will adversely affect the immune or endocrine systems. Therefore, the Agency is not requiring information on endocrine effects of this biochemical pesticide at this time.

**C. ENVIRONMENTAL ASSESSMENT**

**1. Ecological Effects /Hazards Assessment**

Platte Chemical Co. requested waivers for avian oral toxicity, avian dietary toxicity, fish toxicity, aquatic invertebrate toxicity, nontarget plant toxicity, nontarget insect toxicity and honeybee toxicity data requirements. Based on the rational submitted to support the waiver requests, the Agency concluded that the end use product Amplify® Sprout Inhibitor will used in well sealed enclosed areas where 2, 6-DIPN vapor would not escape to avoid compromising the product efficacy. As a result, when the product is used according to the proposed label directions, no direct exposure of birds, aquatic organisms and non-target insect to 2, 6-DIPN is expected to occur. Moreover, there is no evidence that suggest that 2, 6-DIPN will have a negative effects on these organisms. As a result, the Agency granted waivers of these data requirements.

**2. Risk Characterization**

The potential for exposure to 2,6-DIPN is minimal because of the indoors use of Amplify® Sprout Inhibitor, in potato storage facilities. Therefore there will be no risks to avian, aquatic, non-target insects, and non-target plants from the use of this pesticide.

**Table 3** Non-Target Toxicity Data - Tier I Guideline Requirements for 2, 6-DIPN:

| Guideline No. | Study | Result | MRID |
|---|---|---|---|
| 154-6 (850.2100) | Avian acute oral | Waived | NA |
| 154-7 (850.2200) | Avian dietary | Waived | NA |
| 154-8 (850.1075) | Freshwater fish $LC_{50}$ | Waived | NA |
| 154-9 (850.1010) | Freshwater invertebrate $LC_{50}$ | Waived | NA |

## D. EFFICACY DATA

No efficacy data were requested to be submitted to the Agency, since the product does not claim public health uses. Registrants are required to have product performance data available, in the event the performance of the product comes into question and the Agency must review the data.

## IV. RISK MANAGEMENT DECISION

### A. Determination of Eligibility for Registration

Section 3(c)(7)(C) of FIFRA provides for the conditional registration of a pesticide containing a new active ingredient (i.e., not contained in any currently registered pesticide) "for a period reasonably sufficient for the generation and submission of required data...on the condition that by the end of such period the Administrator receives such data and the data do not meet or exceed risk criteria" identified in regulations issued under FIFRA "and on such other conditions as the Administrator may prescribe." Such a conditional registration will be granted "only if the Administrator determines that use of the pesticide during such period will not cause any unreasonable adverse effect on the environment, and that use of the pesticide is in the public interest." EPA has determined that the material 2,6-DIPN is eligible for a conditional registration when used in a aerosol fogging application to potatoes stored in standard commercial potato warehouses and will not likely cause any unreasonable adverse effect on the environment. Registered uses are listed in Table 3, Appendix A

### B. Regulatory Position

#### 1. Conditional Registration

Data submitted are sufficient for a conditional registration of 2,6-DIPN for use as a sprout suppressant of stored potatoes. As a condition of the registration, the Agency requires an enforcement analytical method for livestock and potatoes to be submitted.

#### 2. Tolerance Assessment

The petition to establish a temporary tolerance for the Section 3 registration of 2,6-DIPN was considered in the light of FQPA requirements. The current database supports the establishment of a temporary tolerance which complies with the requirements of FQPA of reasonable certainty will result to the U.S. population including infants and children from aggregate exposure to residues of 2,6-DIPN, including anticipated dietary exposures and all other exposures for which there is reliable information. EPA has arrived at this conclusion based on the toxicity and residue and processing data. A final rule which establishes this temporary tolerance for residues of 2,6-DIPN at 0.5 & 3ppm in or on whole and potato peels was published on August 08, 2003 in the Federal Register concurrent with this Secton 3(c)(7)(C) conditional registration (68 FR 47246).

**3. Codex Harmonization**

There are no Codex harmonization issues since there is no Codex Maximum Residue Limits set for residues of this active ingredient.

**4. Nonfood/Food Registrations**

This active ingredient is to be registered for use on stored potatoes.

**5. Risk Mitigation**

There are no significant risk issues. Applicators and other handlers must wear appropriate personal protective equipment (PPE) such as long-sleeved shirt and long pants, and shoes plus socks and must use a specified filtering respirator in order to mitigate potential occupational exposure and risk to pesticide handlers. Use of this pesticide is restricted to potato warehouses, thus mitigating risks to nontarget organisms. The product label bears appropriate Environmental Hazards text to mitigate any potential risk to fish and aquatic invertebrates.

**6. Endangered Species Statement**

Currently, the Agency is developing a program (The Endangered Species Protection Program) to identify all pesticides whose use may cause potential adverse impacts on endangered and threatened species and their habitats. To aid in the identification of threatened and endangered species and their habitats, several companies have formed an Endangered Species Task Force (EST) under the direction of the American Crop Protection at the subcounty level, and, particularly, if an endangered species occurs in areas where pesticides would be used. This information will be useful once the Endangered Species Protection Program has been implemented.

The Agency has no evidence to believe that any endangered or threatened species will be adversely affected if products containing 2,6-DIPN are used as labeled. In this regard labeling specific for endangered or threatened species is not imposed at this time for such products.

**C. LABELING RATIONALE**

It is the Agency's position that the labeling for 2,6-DIPN complies with the current pesticide labeling requirements. The technical grade product and the end use product are the same.

## 1. Human Health Hazard

### a. Worker Protection Standard

Any product whose labeling reasonably permits its use in an agricultural plant (including potato warehouses) on any farm, forest, nursery, or greenhouse must comply with the labeling requirements of PR Notice 93-7, ''Labeling Revisions required by the Worker Protection Standard (WPS)", and PR Notice 93-11 "Supplemental Guidance for PR Notice 93-7", which reflect the requirements of EPA's labeling regulations for worker protection statements (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170) and must be completed in accordance, and within the deadlines specified in, PR Notices 93-7 and 93-11. Unless otherwise specifically directed, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those Notices. After October 23, 1995, except as provided in PR Notices 93-7 and 93-11, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by any person. The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices. Labeling must also conform to Worker Protection Safety standards concerning re-entry into sprayed fields.

The product label for 2,6-DIPN instructs: "Applicators and other handlers must wear long sleeved shirt and long pants, and shoes plus socks and use a respirator (MSHA/NIOSH approval number prefix N-95,R-95, or P-95)." The product label designates no restricted re-entry period; it states in the Agriculture Use Requirements box "The minimum restricted-entry interval is zero."

### b. Non-worker Protection Standard

There are no non-WPS human health hazard issues for this product.

### c. Precautionary Labeling

The Agency has examined the toxicological data base for 2,6-DIPN, the product Amplify® Sprout Inhibitor based on it, and concluded that the precautionary labeling (i.e. Signal Word, First Aid Statement or lack thereof, and other label statements) adequately mitigates any risks associated with the proposed uses.

For 2,6-DIPN the Signal Word is "CAUTION". First Aid Statements were not required since the pesticide has a Toxicology IV profile. The personal protective equipment has been covered above under the topic "Worker Protection Standard". There is no restricted re-entry interval.

### d. Spray Drift Advisory

No spray drift advisory is required for this use. Use of the product is limited to direct application to stored potatoes under enclosed conditions.

## 2. Environmental Hazards Labeling

Product Environmental Hazards Labeling: 2,6-DIPN is intended for use as a direct application to stored potatoes in potato warehouses. However, the following statements are required on the label of this product. "Do not contaminate water supplies when cleaning equipment or disposing of equipment wash waters. This product may be toxic or pathogenic to fish and aquatic invertebrates. The potential effects of this product on non-target beneficial insects that may be used in greenhouse Integrated Pest Management Programs are not known."

**3. Application Rate**

It is the Agency's position that the labeling for the pesticide Amplify® Sprout Inhibitor, which contains 2,6-DIPN, complies with the current pesticide labeling requirements. For use, the label directs the user to apply up to a maximum of 1 lb. of active ingredient material per 600 lb. of potatoes cwt.

**D. LABELING**

The end use product, Amplify® Sprout Inhibitor and the Technical Grade Active Ingredient (TGAI) 2,6-DIPN are one in the same substance.

Product Name: Amplify® Sprout Inhibitor

ACTIVE INGREDIENT
2,6-Diisopropylnaphthalene.....99.7 %
Other Ingredients.....0.3 %
TOTAL.....100 %

Signal word is "CAUTION", based on the HUMAN HEALTH ASSESSMENT of the product as a Toxicity Category IV substance.

All end-use product labels shall comply with Agency labeling requirements and must contain the following information:

- Product name
- Ingredient Statement
- Registration Number
- "Keep out of reach of children"
- Signal Word (depending on the formulation)
- Precautionary Statements

## V. ACTIONS REQUIRED BY REGISTRANTS

Reports of incidences of adverse effects to humans or domestic animals are required under FIFRA, Section 6(a)2 and incidents of hypersensitivity under 40 CFR Part 158.690), guideline reference number 152-A-15 and OPPTS guideline number 885.3400. Before releasing these products for shipments, the registrant is required to provide appropriate labels and other Agency requirements as discussed in this BRAD and Agency communications.

## VI. APPENDICES

### A. APPENDIX A: Use Site Registration/Reregistration

This is a new active ingredient and not subject to reregistration. Table 3 lists the use sites which can be treated with products containing the active ingredient, 2,6-DIPN. The label for the end-use product is attached.

**Table 4. Use Sites**

| **Amplify® Sprout Inhibitor** | **Official date registered:** |
|---|---|
| **Food use sites**<br>Potato in storage warehouses. | **July 31, 2003** |

## APPENDIX B: BIBLIOGRAPHY

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