United States
Environmental Protection
Agency

Prevention, Pesticides
And Toxic Substances
(7508W)

EPA738-R-97-010
April 1998

Reregistration Eligibility Decision (RED)

Diphenylamine

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

I am pleased to announce that the Environmental Protection Agency has completed its reregistration eligibility review and decisions on the pesticide chemical case diphenylamine which includes the active ingredient N-phenylbenzeneamine. The enclosed Reregistration Eligibility Decision (RED), which was approved on **September 30, 1997** contains the Agency's evaluation of the data base of these chemicals, its conclusions of the potential human health and environmental risks of the current product uses, and its decisions and conditions under which these uses and products will be eligible for reregistration. The RED includes the data and labeling requirements for products for reregistration. It may also include requirements for additional data (generic) on the active ingredients to confirm the risk assessments.

To assist you with a proper response, read the enclosed document entitled "Summary of Instructions for Responding to the RED." This summary also refers to other enclosed documents which include further instructions. You must follow all instructions and submit complete and timely responses. **The first set of required responses is due 90 days from the receipt of this letter. The second set of required responses is due 8 months from the date of this letter.** Complete and timely responses will avoid the Agency taking the enforcement action of suspension against your products.

Please note that the Food Quality Protection Act of 1996 (FQPA) became effective on August 3, 1996, amending portions of both pesticide law (FIFRA) and the food and drug law (FFDCA). This RED takes into account, to the extent currently possible, the new safety standard set by FQPA for establishing and reassessing tolerances. However, it should be noted that in continuing to make reregistration determinations during the early stages of FQPA implementation, EPA recognizes that it will be necessary to make decisions relating to FQPA before the implementation process is complete. In making these early case-by-case decisions, EPA does not intend to set broad precedents for the application of FQPA. Rather, these early determinations will be made on a case-by-case basis and will not bind EPA as it proceeds with further policy development and any rulemaking that may be required.

If EPA determines, as a result of this later implementation process, that any of the determinations described in this RED are no longer appropriate, the Agency will pursue whatever action may be appropriate, including but not limited to reconsideration of any portion of this RED.

If you have questions on the product specific data requirements or wish to meet with the Agency, please contact the Special Review and Reregistration Division representative C.P. Moran at (703) 308-8590. Address any questions on required generic data to the Special Review and Reregistration Division representative Ben Chamblis at (703)308-8174.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
Reregistration Division

Enclosures

SUMMARY OF INSTRUCTIONS FOR RESPONDING TO THE REREGISTRATION ELIGIBILITY DECISION (RED)

1. **DATA CALL-IN (DCI) OR "90-DAY RESPONSE"**--If **generic data** are required for reregistration, a DCI letter will be enclosed describing such data. If **product specific data** are required, a DCI letter will be enclosed listing such requirements. If **both generic and product specific data** are required, a combined Generic and Product Specific DCI letter will be enclosed describing such data. However, if you are an end-use product registrant only and have been granted a generic data exemption (GDE) by EPA, you are being sent only the **product specific** response forms (2 forms) with the RED. Registrants responsible for generic data are being sent response forms for both generic and product specific data requirements (4 forms). **You must submit the appropriate response forms (following the instructions provided) within 90 days of the receipt of this RED/DCI letter; otherwise, your product may be suspended.**

2. **TIME EXTENSIONS AND DATA WAIVER REQUESTS**--No time extension requests will be granted for the 90-day response. Time extension requests may be submitted only with respect to actual data submissions. Requests for time extensions for product specific data should be submitted in the 90-day response. Requests for data waivers must be submitted as part of the 90-day response. All data waiver and time extension requests must be accompanied by a full justification. All waivers and time extensions must be granted by EPA in order to go into effect.

3. **APPLICATION FOR REREGISTRATION OR "8-MONTH RESPONSE"--You must submit the following items for each product within eight months of the date of this letter (RED issuance date).**

a. **Application for Reregistration** (EPA Form 8570-1). Use only an original application form. Mark it "Application for Reregistration." Send your Application for Reregistration (along with the other forms listed in b-e below) to the address listed in item 5.

b. **Five copies of draft labeling** which complies with the RED and current regulations and requirements. Only make labeling changes which are required by the RED and current regulations (40 CFR 156.10) and policies. Submit any other amendments (such as formulation changes, or labeling changes not related to reregistration) separately. You may, but are not required to, delete uses which the RED says are ineligible for reregistration. For further labeling guidance, refer to the labeling section of the EPA publication "General Information on Applying for Registration in the U.S., Second Edition, August 1992" (available from the National Technical Information Service, publication #PB92-221811; telephone number 703-487-4650).

c. **Generic or Product Specific Data**. Submit all data in a format which complies with PR Notice 86-5, and/or submit citations of data already submitted and give the EPA identifier (MRID) numbers. Before citing these studies, you must **make sure that they meet the Agency's acceptance criteria** (attached to the DCI).

d. **Two copies of the Confidential Statement of Formula (CSF)** for each basic and each alternate formulation. The labeling and CSF which you submit for each product must comply with P.R. Notice 91-2 by declaring the active ingredient as the **nominal concentration**. You have two options for submitting a CSF: (1) accept the standard certified limits (see 40 CFR §158.175) or (2) provide certified limits that are supported by the analysis of five batches. If you choose the second option, you must submit or cite the data for the five batches along with a certification statement as described in 40 CFR §158.175(e). A copy of the CSF is enclosed; follow the instructions on its back.

e. **Certification With Respect to Data Compensation Requirements**. Complete and sign EPA form 8570-31 for each product.

4. **COMMENTS IN RESPONSE TO FEDERAL REGISTER NOTICE**--Comments pertaining to the content of the RED may be submitted to the address shown in the Federal Register Notice which announces the availability of this RED.

5. **WHERE TO SEND PRODUCT SPECIFIC DCI RESPONSES (90-DAY) AND APPLICATIONS FOR REREGISTRATION (8-MONTH RESPONSES)**

By U.S. Mail:

Document Processing Desk **(RED-SRRD-PRB)**
Office of Pesticide Programs (7504C)
EPA, 401 M St. S.W.
Washington, D.C. 20460-0001

By express:

Document Processing Desk **(RED-SRRD-PRB)**
Office of Pesticide Programs (7504C)
Room 266A, Crystal Mall 2
1921 Jefferson Davis Hwy.
Arlington, VA 22202

6. **EPA'S REVIEWS**--EPA will screen all submissions for completeness; those which are not complete will be returned with a request for corrections. EPA will try to respond to data waiver and time extension requests within 60 days. EPA will also try to respond to all 8-month submissions with a final reregistration determination within 14 months after the RED has been issued.

REREGISTRATION ELIGIBILITY DECISION

DIPHENYLAMINE

LIST B

CASE 2210

ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
SPECIAL REVIEW AND REREGISTRATION DIVISION

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DIPHENYLAMINE REREGISTRATION ELIGIBILITY DECISION TEAM

Office of Pesticide Programs:

Biological and Economic Analysis Assessment

George Keitt	Biological Analysis Branch
Alan Halverson	Economic Analysis Branch

Environmental Fate and Effects Risk Assessment

Richard Lee	Environmental Risk Branch IV
Jose Melendez	Environmental Risk Branch IV
Mary Frankenberry	Environmental Risk Branch III
Miachel Rexrode	Environmental Risk Branch IV

Health Effects Risk Assessment

Christina Swartz	Reregistration Support Chemistry Branch
Monica Spann	Occupational and Residential Exposure Branch
Stephen C. Dapson	Toxicology Branch II
Brian Steinwand	Dietary Risk Analysis/SAB
Robert Travaglini	Risk Characterization and Analysis Branch

Registration Support Risk Assessment

John Bazuin	Fungicide-Herbicide Branch

Risk Management

Ben Chambliss, Team Leader	Reregistration Branch I

GLOSSARY OF TERMS AND ABBREVIATIONS

ADI	Acceptable Daily Intake. A now defunct term for reference dose (RfD).
AE	Acid Equivalent
a.i.	Active Ingredient
ARC	Anticipated Residue Contribution
CAS	Chemical Abstracts Service
CI	Cation
CNS	Central Nervous System
CSF	Confidential Statement of Formula
DFR	Dislodgeable Foliar Residue
DRES	Dietary Risk Evaluation System
DWEL	Drinking Water Equivalent Level (DWEL) The DWEL represents a medium specific (i.e. drinking water) lifetime exposure at which adverse, non carcinogenic health effects are not anticipated to occur.
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End-Use Product
EPA	U.S. Environmental Protection Agency
FAO/WHO	Food and Agriculture Organization/World Health Organization
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GLC	Gas Liquid Chromatography
GM	Geometric Mean
GRAS	Generally Recognized as Safe as Designated by FDA
HA	Health Advisory (HA). The HA values are used as informal guidance to municipalities and other organizations when emergency spills or contamination situations occur.
HDT	Highest Dose Tested
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LD_{lo}	Lethal Dose-low. Lowest Dose at which lethality occurs.
LEL	Lowest Effect Level
LOC	Level of Concern
LOD	Limit of Detection
LOEL	Lowest Observed Effect Level
MATC	Maximum Acceptable Toxicant Concentration
MCLG	Maximum Contaminant Level Goal (MCLG) The MCLG is used by the Agency to regulate contaminants in drinking water under the Safe Drinking Water Act.
µg/g	Micrograms Per Gram
μg/L	Micrograms per liter
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MP	Manufacturing-Use Product
MPI	Maximum Permissible Intake
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.

GLOSSARY OF TERMS AND ABBREVIATIONS

N/A	Not Applicable
NOEC	No Observable Effect Concentration
NPDES	National Pollutant Discharge Elimination System
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
OP	Organophosphate
OPP	Office of Pesticide Programs
Pa	pascal, the pressure exerted by a force of one newton acting on an area of one square meter.
PADI	Provisional Acceptable Daily Intake
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRN	Pesticide Registration Notice
Q^*_1	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RS	Registration Standard
RUP	Restricted Use Pesticide
SLN	Special Local Need (Registrations Under Section 24 (c) of FIFRA)
TC	Toxic Concentration. The concentration at which a substance produces a toxic effect.
TD	Toxic Dose. The dose at which a substance produces a toxic effect.
TEP	Typical End-Use Product
TGAI	Technical Grade Active Ingredient
TLC	Thin Layer Chromatography
TMRC	Theoretical Maximum Residue Contribution
torr	A unit of pressure needed to support a column of mercury 1 mm high under standard conditions.
WP	Wettable Powder
WPS	Worker Protection Standard

EXECUTIVE SUMMARY

The U. S. Environmental Protection Agency has completed its reregistration eligibility decision of the pesticide diphenylamine. This decision includes a comprehensive reassessment of the required target data and the use patterns of currently registered products.

Diphenylamine is a plant growth regulator used post-harvest on apples to control storage scald. This end-use pattern for the current formulations has been classified as indoor food use, and applications include tank dipping, drenching, conveyor flooding, and spraying. It is formulated as a wettable powder, as an emulsifiable concentrate, a soluble concentrate/liquid and liquid ready-to-use. The Diphenylamine Task Force is supporting the reregistration of diphenylamine for use only in the prevention of storage scald on apples prior to entering storage.

The Agency has concluded that all uses, as prescribed in this document, will not cause unreasonable risks to humans or the environment. Therefore, all products containing diphenylamine are eligible for reregistration.

In reaching the determination of safety for infants and children, the Agency found that the toxicity data base for diphenylamine is complete, based on current requirements, and the effects observed in pre- and post-natal studies do not indicate an increased sensitivity of infants and children to diphenylamine. Therefore, an additional uncertainty factor to account for any special sensitivity to infants and children was not warranted for diphenylamine and nitrosamine (TGAI impurity) and was not used in the risk assesment.

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and other exposures for which there is reliable information. Since there are no data on diphenylamine in the Agency's Pesticides in Ground Water Database or in the U.S. EPA's "STORET" database, and the limited use pattern which is unlikely to result in DPA residues in drinking water, dietary risk from drinking water will be assumed to be negligible. Diphenylamine is a food use chemical. There are no residential (non-occupational) uses of diphenylamine; therefore, the considerations for aggregate exposure are those only from food. Since the only aggregate concern is dietary and all chronic risk fall below 100 % RfD, there is no aggregate chronic dietary risk concern for diphenylamine. An acute dietary risk assessment was not conducted since no appropriate endpoint was identified in the available studies.

EPA does not have, at this time, available data to determine whether diphenylamine has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this reregistration decision, EPA has not assumed that diphenylamine has a common mechanism of toxicity with other substances.

Because of minimal expected adverse risk on ecological systems and due to the unlikeliness of exposure, risk to endangered species is not expected.

Before reregistering the products containing diphenylamine, the Agency is requiring that product specific data, revised Confidential Statements of Formula (CSF) and revised labeling be

submitted within eight months of the issuance of this document. These data include product chemistry for each registration and acute toxicity testing. After reviewing these data and any revised labels and finding them acceptable in accordance with Section 3(c)(5) of FIFRA, the Agency will reregister a product. Those products which contain other active ingredients will be eligible for reregistration only when the other active ingredients are determined to be eligible for reregistration.

I. INTRODUCTION

In 1988, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act provides a schedule for the reregistration process to be completed in nine years. There are five phases to the reregistration process. The first four phases of the process focus on identification of data requirements to support the reregistration of an active ingredient and the generation and submission of data to fulfill the requirements. The fifth phase is a review by the U.S. Environmental Protection Agency (referred to as "the Agency") of all data submitted to support reregistration.

FIFRA Section 4(g)(2)(A) states that in Phase 5 "the Administrator shall determine whether pesticides containing such active ingredient are eligible for reregistration" before calling in data on products and either reregistering products or taking "other appropriate regulatory action." Thus, reregistration involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criterion of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) (Public Law 104-170) was signed into law. FQPA amends both the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 301 *et seq*., and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136 *et seq*. The FQPA amendments went into effect immediately. As a result, EPA is embarking on an intense process, including consultation with registrants, States, and other interested stakeholders, to make decisions on the new policies and procedures that will be appropriate as a result of FQPA. This process will include a more in depth analysis of the new safety standard and how it should be applied to both food and non-food pesticide applications. The FQPA did not, however, amend any of the existing reregistration deadlines in section 4 of FIFRA. The Agency will therefore continue its ongoing reregistration program while it continues to determine how best to implement FQPA.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of diphenylamine (DPA). The document consists of six sections. Section I is the introduction. Section II describes diphenylamine, its uses, data requirements and regulatory history. Section III discusses the human health and environmental assessment based on the data available to the Agency. Section IV presents the reregistration decision for diphenylamine. Section V discusses the reregistration requirements for diphenylamine. Finally, Section VI is the Appendices which support this Reregistration Eligibility Decision. Additional details concerning the Agency's review of applicable data are available on request.

II. CASE OVERVIEW

A. Chemical Overview

The following active ingredient(s) are covered by this Reregistration Eligibility Decision:

- **Common Name:** Diphenylamine (DPA)
- **Chemical Name:** N-phenylbenzeneamine
- **CAS Registry Number:** 122-39-4
- **OPP Chemical Code:** 038501
- **Empirical Formula:** $C_{12}H_{11}N$
- **Trade and Other Names:** DPA, Shield DPA, Big Dipper, Decoscald 282, and No Scald DPA 283
- **Basic Manufacturer:** Elf Atochem and Pace International

B. Use Profile

The following is information on the currently registered uses with an overview of use sites and application methods. A detailed table of the uses of diphenylamine are in Appendix A.

For Diphenylamine:

Type of Pesticide: plant growth regulator

Use Sites: apples

Target Pests: storage scald

Formulation Types Registered: emulsifiable concentrate, liquid ready-to-use soluable concentrate, wettable powder

Methods and Rates of Application:

Equipment: drencher, tank

Method and Rate: Dip treatment, Post-harvest, Tank
2.666 lb/159 gal; 1.66 lb/100 gal

Drench, Post-harvest, Drencher
2.666 lb/159 gal

Flood treatment, Post-harvest, Conveyer
1.66 lb/100 gal

Spray, Post-harvest, Sprayer
1.66 lb/100 gal

Spray, Post-harvest, Sprayer
2.666 lb/159 gal

Timing: post-harvest

C. Estimated Usage of Pesticide

This section summarizes the best estimates available for the pesticide uses of diphenylamine. These estimates are derived from a variety of published and proprietary sources available to the Agency. The data, reported on an aggregate and site (crop) basis, reflect annual fluctuations in use patterns as well as the variability in using data from various information sources.

Based on available pesticide usage and residue data for 1990 through 1994, an annual estimate of the total domestic usage of diphenylamine is approximately one hundred thousand pounds of active ingredient (a.i.) applied post-harvest to approximately 1.8 million tons of apples. The average treatment rate for post-harvest apples is about 0.04 pounds a.i. per ton. Much of the diphenylamine usage occurs in Washington, New York, Michigan and California.

Table 1: Annual Usage of Diphenylamine Based on 1989-1994 Data
Post-Harvest Production Treated

Site	Utilized Production (Tons)	Tons Treated		% of Crop Treated		LB AI Applied		Avg. Appl. Rates		States of Most Usage
		Likely Average	Likely Max	Likely Average	Likely Max	Likely Average	Likely Max	lb ai/ ton/yr	# appl /year	
Apples, U..S.	5,367,600	1,775,630	1,866,460	33	35	74,370	94,370	0.042	1	(WA, NY, MI, CA): 93%
Apples, CA	461,670	51,120	77,460	11	17	3,440	5,840	0.067	1	CA: 100%

Notes:
- Percent of U.S. apples treated post-harvest estimated as: (total no. of detects of residues in 14 states)/(total sample size in 14 states)*100.
- Pounds a.i. applied to U.S. aples post-harvest estimated as: (total no. of detects in 14 states)*(lbs. a.i. applied in CA)/(no. of detects in CA).
- Data in the table may not exactly multiply or divide across because of rounding.

Sources:
- California EPA, California Use Reports, Annuals 1990-1994.
- US Department of Commerce/Bureau of the Census, 1992 Census of Agriculture, New Hampshire State and County Data.
- US EPA proprietary sources.
- USDA Pesticide Data Program (PDP) database, 1992 and 1993.
- USDA/ERS, Fruit and Tree Nuts, Situation and Outlook Report, August 1992.
- USDA/NASS, Noncitrus Fruits and Nuts, 1993 Preliminary and 1994 Summary.

D. Data Requirements

Appendix B includes all data requirements identified by the Agency for the currently registered uses of diphenylamine needed to support reregistration.

E. Regulatory History

The first product containing diphenylamine (DPA), Franklin Protec (Reg. No. 410-12), was registered on 26 December 1947 by Franklin Laboratories, Inc. for use against maggots and screw worms on horses. In early 1948, two other companies, C.J. Martin Company and Texas Phenothiazine Company, registered one DPA product each, Martin's Formula No. 62 Screwworm Smear for Horses and Mules (Reg. No. 299-2) and Dr. Rogers's Screwworm Smear Formula No. 62 (Reg. No. 327-26), respectively, for screw worm control on both horses and work mules. A DPA product, Diphenylamine 83-W (Reg. No. 241-69), was first registered by American Cyanamid Company, for use against storage scald on apples on February 14, 1962. A number of additional products were subsequently registered for this site and pest between April, 1962 and the end of 1981. In 1963, a DPA-containing product, Grosley's Original "No-roost" Bird Repellent (Reg. No. 7682-1), was first registered by Aegis Labs, Inc. as a bird repellant for use in residential outdoor and commercial areas, and bird roosting and nesting areas. A second product, Tower Grezall NP-4 Bird Repellent (Reg. No. 10286-1) was registered by Tower Oil Company for these purposes in 1968. In early 1985, the most recent new Section 3 DPA-containing product, DPA Oiled White Paper (Reg. No. 51650-1), was registered by Compania Manufactura de Papeles y Cartones, S.A., for use on fruit wrappers against fungi, a new pest use.

The only two DPA-containing Special Local Needs product registrations were issued to Washington state in 1994 for use on apples. However, in early 1976 an old Intrastate product was registered for screwworm control. These registrations have expired and are no longer active.

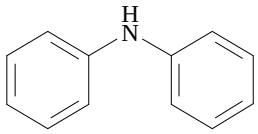
Elimination of uses began in July, 1986 when Franklin Protec, the product with the maggot control use was cancelled. In October, 1989 all of the products labeled for screwworm control, the fungi in fruit wrapper use, and bird repellency were cancelled.

Currently only three DPA-containing products are active. One is a purified technical product (Reg. No. 2792-47) for use in the formulation of other products, while the other two products (Reg. No. 2792-45 and 64864-3) are registered for use against storage scald on apples.

III. SCIENCE ASSESSMENT

A. Physical Chemistry Assessment

The physical and chemical characteristics of diphenylamine are described below:



Empirical Formula:	$C_{12}H_{11}N$
Molecular Weight:	169.22
CAS Registry No.:	122-39-4
Shaughnessy No.:	038501

Below is a description of the physical and chemical properties of the technical grade of diphenylamine.

Color:	cream
Physical State:	solid flake with a sharp creosote odor
Melting Point:	53-55°C
Solubility:	water at 0.038-0.042 mg/mL acetonitrile at 808-897 mg/mL methanol at 454-492 mg/mL octanol at 204-237 mg/mL hexane at 53-66 mg/mL

B. Human Health Assessment

1. Hazard Assessment

The toxicological database for diphenylamine is adequate to support a reregistration eligibility.

a. Acute Toxicity

The Agency has characterized the acute toxicity of technical grade diphenylamine based on laboratory data. Results of the acute toxicity studies conducted with diphenylamine are summarized in Table 2:

Table 2. Acute Toxicity Values of Diphenylamine.

Test	Purity (% a.i.)	Results	Cat
Oral LD_{50}--rat	99.9%	LD_{50} = 2.72(2.49-2.98) g/kg	III
Dermal LD_{50}--rabbit	99.9%	LD_{50} > 2 g/kg	III
Inhalation LC_{50}--rat	EC-283 (31.0%)	LC_{50} = 1.46 mg/L	III
Eye irritation--rabbit[a]	99.9%	Slight eye irritation	III
Dermal irritation--rabbit[a]	99.9%	Slight skin irritation	III
Dermal sensitization guinea pig[a]	99.9%	Not a dermal sensitizer	NA

[a] Not required for TGAI, however, presented here for informational purposes.

b. Subchronic Toxicity

In a subchronic oral toxicity study, Sprague Dawley rats (10 rats/sex/group) received diphenylamine technical (> 99%) at dietary dose levels of 0, 150, 1500, 7500, or 15000 ppm for 90 days (approximately 0, 7.5, 75, 375, or 750 mg/kg/day). There were a number of significant dose-related effects. A greenish tint to the animals' fur appeared first in the females (90%) in the 1500 ppm dose level group. Sixty percent of the males and 100% of the females showed this same greenish tint at 7500 ppm. At the highest dose tested (15000 ppm) 70% of the males and 100% and females the greenish tinted-hair respectively. Body weights and body weight gains were reduced in both sexes in the 7500 and 15000 ppm dose groups throughout the time-course of the study without compromising food consumption, therefore, suggesting decreased food efficiency. The darkening of the urine was considered to be a significant treatment-related graded dose-response effect. Compared to the concurrent controls, 60% of the males excreted dark yellow urine at 7500 ppm, and 100% of the animals excreted dark yellow urine at 15000 ppm. Pairwise, in the females at 7500 or 15000 ppm, the percentage of rats that excreted dark yellow urine was 70% and 100% respectively.

In general, there were significant treatment-related effects on the hematology parameters evaluated at terminal sacrifice that became apparent at a lower dose level. These treatment-related effects on more parameters were observed in females than in males when compared to the concurrent controls. The hematological changes observed in males at 7500 and 15000 ppm were statistically significant showing decreases in Red Blood Cell (RCB) and Hemoglobin (HGB) counts, and increases in Mean Corpuscular Volume (MCV) and Mean Cell Hematocrit (MCH). In females at 1500, 7500, and 15000 ppm, diphenylamine caused decreases in RBC, HGB, and Hematocrit counts and increases in MCV and MCH. The NOEL was 75 mg/kg/day for males and 7.5 mg/kg/day for females. The LOEL was 375 mg/kg/day for males and 75 mg/kg/day for females based on increased clinical signs of toxicity and alterations in hematological parameters (MRID 42339701).

In a subchronic toxicity study, pure-bred beagle dogs (4/sex/dose) received gelatin capsules containing diphenylamine technical (> 99%) at dose levels of 0, 5, 25, or 50 mg/kg/day for at least 90 days. None of the dogs died during the study. The statistically significant increases observed only in a few of the hematology and clinical chemistry parameters were not considered to be toxicologically or biologically relevant. The NOEL was equal to or greater than 50 mg/kg/day which was the Highest Dose Tested (HDT). A LOEL was not established (MRID 42339801).

In a subchronic toxicity, CD-1 mice (15/sex/dose) received technical diphenylamine (> 99%) in their diet at 0, 10, 525, 2625 or 5250 ppm for 90 days. The dosages consumed in mg/kg/day for males and females, respectively, were 1.7 and 2.1 at 10 ppm, 93.8 and 107.0 at 525 ppm, 443.5 and 555.5 at 2625 ppm and 925.8 and 1100.7 at 5250 ppm. Slight treatment-related effects were observed at 525 ppm with the appearance of brownish-yellow pigment and extra-medullary hematopoiesis in the liver and hemosiderosis, congestion and extramedullary hematopoiesis in the spleen. As the dosage was increased, not only were the incidence and severity of the lesions in the spleen and liver increased, but pigment in kidneys, increased cellularity in the bone marrow, and cystitis (in the 5250 ppm group) were also present. Treatment-related increases in relative organ weights were seen in the liver and spleen in the highest dose groups (2625 and 5250 ppm). Hematology parameters showing treatment-related effects included statistically significant decreases in RBC count and hematocrit. Also statistically significant increases in MCV, MCH and MCHC in the two highest dosage groups were observed. The highest dosage group also showed a marked increase in reticulocytes. In the 525 ppm group, there was a statistically significant increase in MCHC. The systemic toxicity NOEL was 10 ppm (1.7 mg/kg/day for males and 2.1 mg/kg/day for females) and the LOEL was 525 ppm (93.8 mg/kg/day for males and 107.0 mg/kg/day for females) (MRID 42542801).

In a 21- day dermal toxicity study, New Zealand White rabbits (5/sex/group) received repeated dermal applications (under occlusion) of diphenylamine technical (100%) dissolved in distilled water at dose levels of 100, 500, or 1000 mg/kg for six hours a day for 21 consecutive days with terminal sacrifice on day 22. Two additional groups of rabbits of each sex (5/sex) served as the vehicle (distilled water) controls. No mortality was noted in the study. Gross pathology was noted as dark-red foci in the stomachs of both sexes at the 500 and 1000 mg/kg/day groups. The systemic toxicity NOEL was 100 mg/kg/day and the LOEL was 500 mg/kg/day based on the effects in the stomach. The dermal toxicity NOEL was greater than 1000 mg/kg/day (limit dose)(MRID 42304901).

c. Chronic toxicity

In a combined chronic feeding/carcinogenicity study, Sprague-Dawley rats received diphenylamine (> 99.0%) at dose levels of 0, 200, 750, 3750 or 7500 ppm in males (equal to 8.1, 28.8, 146.7, or 302.1 mg/kg/day) and 0, 150, 500, 2500, or 5000 ppm in females (equal to 7.5, 24.9, 137.8, or 286.1 mg/kg/day) in the diet for 2 years. A one year interim sacrifice of 10 animals per sex per dose group was used. There was no treatment related mortality noted, however, the study was terminated early due to increased mortality in the control and low dose animals. No effects were noted in ophthalmic examinations. The only treatment related clinical observation was a greenish tint to the hair coat in the urogenital or ventral cervical area which was assumed to be due to an…*oxidative product of the interaction of the test article or a metabolite with urine or feces* in the high mid and high dose groups. Systemic toxicity was noted at the high mid and high dose groups in both sexes as decreased mean body weights and body weight gains (statically significant). Food consumption was increased in the same dose groups; however, due to food spillage, when food consumption values exceeded two standard deviations from the mean, they were not included in calculation of the group mean food consumption. Treatment related effects were noted in hematology involving *red cell elements* mainly in the high mid and high dose groups. Increases in albumin levels, decreases in globulin levels and increased albumin/globulin ratios were noted but, the biological relevance to these changes is unknown since there was no related pathology. Some slight transient effects were also noted in alkaline phosphatase and total bilirubin also in serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT). Urinalysis did not reveal any specific treatment related effects except a slight increase in ketones in the high dose due to incomplete or partial interference of the test article causing a false positive reading. There was an increase in spleen weights in both sexes in the high mid and high dose groups at the interim sacrifice and terminal sacrifice. Gross necropsy observations revealed a roughened surface to the kidneys in the high dose groups. Treatment related non-neoplastic observations were splenic congestion, increased hemosiderosis and hematopoiesis in the spleen, pigment deposits in the kidneys, and increased hematopoiesis in the liver in the high mid and high dose groups. No treatment related increase in any tumor type or site was seen in either sex at any dose level. Methemoglobin was not measured in this study. For chronic toxicity the NOEL was 28.8 mg/kg/day in males and 24.9 mg/kg/day in females and the LOEL was 146.7 mg/kg/day in males and 137.8 mg/kg/day in females based on reduced mean body weight and body weight gains, changes in hematological parameters, splenic and kidney lesions and increased clinical signs of toxicity. There was no evidence of carcinogenicity (MRID 43401401).

In a chronic toxicity study, beagle dogs received by capsule either 0, 10, 50, or 100 mg/kg/day of diphenylamine sodium salt (> 99%) for 12 months.

Systemic toxicity was noted at the 10 mg/kg/day dose group, lowest dose tested (LDT), and above as alterations in clinical chemistry. There was a dose-related increase in total bilirubin levels in both sexes for the 10 mg/kg/day, up to 75% for the 50 mg/kg/day, up to 167%, $p < 0.01$ and for the 100 mg/kg/day groups, up to 150%, $p < 0.01$. These increases showed statistical significance in both sexes in the 10 mg/kg/day group at week 26 and in females only at week 39. Also, there was a decrease in blood urea nitrogen (BUN) levels in females at 50 mg/kg/day (16%) and 100 mg/kg/day (20%) groups at week 52. Cholesterol was increased at 50 mg/kg/day and 100 mg/kg/day at all time points (4 to 68%; occasionally $p < 0.05$), and albumin showed occasional increases, although no differences were noted at the end of the study. Alterations seen in the hematological parameters included: a treatment related decrease in red blood cells at 100 mg/kg/day (11%; $p < 0.05$ in males at 52 weeks). Also, hemoglobin was slightly reduced in both sexes at 100 mg/kg/day (males, 7-9%; females, 4-7%), hematocrit was slightly reduced at 100 mg/kg/day males (5-9%), mean corpuscular volume was slightly increased in both sexes at 100 mg/kg/day (males, 2-4%; females, 6%), and platelets were increased in all treated males (3-35%; $p < 0.05$ to 0.01 at various time points). The absolute and relative kidney weights were increased in males at 50 mg/kg/day (40/36%) and 100 mg/kg/day (18/10%) and in females at both 50 mg/kg/day (24/13%) and 100 mg/kg/day (13/9%). The absolute and relative liver weights were increased at 50 mg/kg/day (males, 17/13%; females, 22/11%) and 100 mg/kg/day (males, 29/20%; females, 14/10%). The absolute and relative spleen weights were increased in all treated females (9 to 38%/11 to 32%) and the thyroid absolute and relative weights were decreased in 100 mg/kg/day females (23/25%), and there were clinical signs where one 50 mg/kg/day and two 100 mg/kg/day animals had a greenish tint to the hair of the feet. Methemoglobin was not measured in this study (see RfD section). For chronic toxicity a NOEL was not achieved; the LOEL was 10 mg/kg/day (LDT) based on alterations in clinical chemistry parameters (MRID 43000601).

d. Carcinogenicity

Diphenylamine

In a carcinogenicity study, CD-1 mice (60 sex/group) were administered diphenylamine (> 99%) in the diet at levels of 0, 525, 2625 or 5250 ppm (males: 73.2, 368.0 and 755.7 mg/kg/day; females: 90.5, 455.2 or 936.6 mg/kg/day) for 18 months. There was a significant treatment-related increase in overall mortality in the 2625 and 5250 ppm group males and females. The increased mortality was due to cystitis in males and amyloidosis in females. A greenish staining of the hair was the most frequently observed clinical sign with some of the 525 ppm group and essentially all of the 2625 and 5250 ppm groups affected by the end of the study. Mean body weight gain was significantly decreased in the 5250 ppm group males at the majority of the time points in the study. Decreases were also

occasionally recorded for the 2625 ppm group males. Changes in the hematology parameters indicate that the chemical produced a regenerative anemia in the 2625 and 5250 ppm group males and females. On gross examination at the interim and terminal necropsies, the liver and spleen of the 2625 and 5250 ppm group animals were dark and enlarged. The absolute and relative weights of the liver and spleen were also increased in these animals. On histopathology at the interim and terminal necropsies, 525 ppm group and above had increased incidence of hemosiderosis and congestion in the spleen, also the 2625 and 5250 ppm groups had increased incidences and/or severity of hematopoiis in the spleen and liver, and pigment in the reticuloendothelial cells of the liver. Pigment was also observed in the convoluted epithelial cells of the kidney of these groups at the terminal necropsy. The incidence of pyelonephritis in the 5250 ppm group males was marginally increased. There were increased incidences of cystitis and dilatation of the urinary bladder and balanoposthitis in the penis and preputial area of the 2625 and 5250 ppm groups at both of the necropsies. For the 5250 ppm group females, the incidence of amyloidosis was increased in the thyroid, adrenals, kidneys (also in the 2625 ppm group), stomach, small intestines, ovaries and uterus. For chronic toxicity the NOEL was less than 525 ppm (73.2 mg/kg/day for males and 90.5 mg/kg/day for females), and the LOEL was equal to or less than 525 ppm (73.2 mg/kg/day for males and 90.5 mg/kg/day for females) based on histopathological lesions in the spleen. There was no evidence of carcinogenicity (MRID 43369501).

Nitrosamine

Based on animal carcinogenicity data, N-nitrosodiphenylamine is classified as a probable human carcinogen. Studies in rats and mice showed increased incidence of bladder tumors in male and female rats and reticulum cell sarcomas in mice as well as structural relationship to carcinogenic nitrosamines. The cancer potency or Q_1 * was calculated to be 4.9×10^{-3} mg/kg/day.

e. Developmental Toxicity

In a developmental toxicity study, pregnant female Sprague-Dawley rats (25/group) received diphenylamine (99.9%) in corn oil by oral gavage at dose levels of 0, 10, 50, or 100 mg/kg/day from gestation day six through gestation day 15 inclusive; dams were sacrificed on gestation day 20. None of the rats died during the study. Maternal toxicity was evidenced by increased splenic weights, enlarged spleens and blackish-purple colored spleen in the dams at 100 mg/kg/day. The maternal toxicity NOEL was 50 mg/kg/day and the LOEL was 100 mg/kg/day. No developmental toxicity was seen at any dose level. The developmental toxicity NOEL was equal to or greater than 100 mg/kg/day (HDT); a LOEL was not established (MRID 42292001).

In a developmental toxicity study, pregnant New Zealand White rabbits received either 0, 33, 100, or 300 mg/kg/day diphenylamine (99.9%) suspended in 1% methylcellulose by oral gavage from gestation day 7 through 19, inclusive. Animals came from 3 sources(vendors). Maternal toxicity was noted at 300 mg/kg as decreases in food consumption and associated initial reductions in body weight gain. The maternal toxicity NOEL was 100 mg/kg/day and the LOEL was 300 mg/kg/day based on decreased body weight gains and food consumption early during the treatment period. No developmental toxicity was noted at any dose level. The developmental toxicity NOEL was equal to or greater than 300 mg/kg/day (HDT); a LOEL was not established (MRID 00148521).

f. Reproductive Toxicity

In a two-generation reproductive toxicity study, Sprague-Dawley rats (28 per sex/group) received diphenylamine (99.8%) in the diet at dose levels of 0, 500, 1500, or 5000 ppm (0, 40, 115, or 399 mg/kg/day for F_0 males and 0, 46, 131, or 448 mg/kg/day for F_0 females, respectively, during premating). Compound-related systemic toxicity was observed in a dose related manner among both sexes and generations at all dose levels. In general, females were more affected than males and F_1 animals were more affected than F_0 animals. Clinical signs (bluish colored fluid in the cage and bluish colored staining of the coat in both sexes, and swelling of mammary gland(s) or palpable lateral-ventral masses, primarily in females) were evident at 5000 ppm. Body weight was decreased at 1500 and 5000 ppm. At 5000 ppm, there was a 6-9% decrease in body weight values, as compared to control, for F_0 males, 5-8% for F_0 females, 22-28% for F_1 males, and 11-23% for F_1 females. At 1500 ppm, there was a 5-8% decrease in body weight values from controls for F_0 females, 7-9% for F_1 males, and 5% for F_1 females. Food consumption (g/animal/day) was also decreased at 1500 and 5000 ppm. Kidney, spleen, and liver appeared to be the target organs as evidenced by weight differences from control at 5000 ppm in males and at 1500 and 5000 ppm in females and gross and microscopic findings at all dose levels in both sexes. Gross findings included enlarged and blackish-purple spleens. Microscopic findings included brown pigment in the proximal convoluted tubules of the kidney, hepatocytic hypertrophy, brown pigments in the Kupffer cells of the liver, congestion and hemosiderosis of the spleen. The systemic toxicity NOEL was less than 500 ppm (40 mg/kg/day in males and 46 mg/kg/day in females). The LOEL was less than or equal to 500 ppm based on gross pathological findings in the spleen (enlarged, discolored), and on microscopic findings in the kidney (brown pigment in the proximal convoluted tubule), liver (hepatic hypertrophy and brown pigment in the Kupffer cells), and spleen (congestion and hemosiderosis).

Developmental toxicity was observed at 1500 and 5000 ppm, as evidenced by significantly decreased body weight for F_1 pups at 5000 ppm throughout lactation (11-25 % less than control), for F_2 pups at 5000 ppm from LD 4 through

LD 21 (10%-29% less than control), and for F_2 pups at 1500 ppm on LD 14 (10%) and LD 21 (12%). The developmental toxicity NOEL was 500 ppm (46 mg/kg/day for maternal animals) and the LOEL was 1500 ppm (131 mg/kg/day for maternal animals) based on decreased F2 pup body weight in late lactation. Reproductive toxicity was noted as smaller litter sizes at birth (significant for the F_2 litters) in both generations at 5000 ppm. The reproductive toxicity NOEL was 1500 ppm (131 mg/kg/day for maternal animals) and the LOEL was 5000 ppm (448 mg/kg/day for maternal animals), based upon decreased litter size in both generations (MRID 42638101).

g. Mutagenicity

In a *Salmonella typhimurium*/mammalian microsome plate incorporation assay with tester strains TA1535, TA1537, TA1538, TA98, and TA100, diphenylamine (99.9%) was found to be cytotoxic at doses $\geq$333 μg/plate -S9, and $\geq$667 μg/plate +S9. At lower levels (6.67, 10.0, 33.3, 66.7, and 100 μg/plate -S9; 10.0, 33.3, 66.7, 100, and 333 μg/plate +S9), there were no increases in histidine-revertant colonies. Based on these findings, it was concluded that diphenylamine was tested over an appropriate range of concentrations, and was not mutagenic in this bacterial test system (MRID 42312101).

In a L5178Y TK+/- mouse lymphoma forward mutation assay, diphenylamine (99.9%) was tested at dose levels of 5-80 μg/mL in DMSO both with and without rat liver S9 metabolic activation. The test was positive in the presence of exogenous metabolic activation. There were reproducible but not dose-related increases in the mutation frequency at severely cytotoxic levels (40-70 μg/mL +S9) and moderately cytotoxic concentrations (20 and 30 μg/mL +S9). Colony sizing analysis revealed a relatively equal distribution of large and small colonies. Diphenylamine was non-mutagenic in the absence of S9 activation up to a severely cytotoxic level (80 μg/mL). Thus, diphenylamine was considered to be weakly mutagenic in this assay (MRID 42332101).

In a mouse micronucleus assay, the single oral gavage administration of 250, 500, or 1000 mg/kg (males) or 375, 750, or 1500 mg/kg (females) diphenylamine (99.9%) did not significantly increase the frequency of micronucleated polychromatic erythrocytes in bone marrow cells harvested from ICR mice at 24, 48, or 72 hours postexposure. Dose selection for the micronucleus assay was based on the findings of a preliminary acute dose range-finding study which indicated that ~70% of the females administered 2750 mg/kg of the test material died prior to the scheduled sacrifice. In agreement with the preliminary results, mortality and other signs of compound toxicity (i.e., languidness, squinted eyes and/or rough fur) were seen in both sexes receiving the high dose (1000 mg/kg; males; 1500 mg/kg; females) in the micronucleus assay. The test was negative up to a lethal oral gavage dose (HTD: 1000 mg/kg; males; 1500 mg/kg; females) but there was no evidence of bone marrow cytotoxicity (MRID 42312001).

The acceptable mutagenicity studies discussed above satisfy the new initial mutagenicity battery requirements for diphenylamine. However, the majority of toxicology studies conducted with diphenylamine indicate that the liver is a target organ. Therefore, the HED RfD/QA Peer Review Committee is requiring an *in vivo*/*in vitro* rat hepatocyte unscheduled DNA synthesis (UDS) assay be performed to determine if a potentially genotoxic concentration can be achieved in the liver. The request for additional testing is in accordance with Agency current mutagenicity guidelines. The outcome of this study will determine if any additional mutagenicity studies are required for diphenylamine.

h. Metabolism

In a general metabolism study in the rat, ^{14}C-Diphenylamine was administered orally in corn oil to groups of male and female Sprague Dawley rats (5/sex/group) at a low oral dose (5 mg/kg), repeated low oral dose (5 mg/kg x 14 days), and a single high oral dose (750 mg/kg).

Absorption of diphenylamine appeared rapid and complete for all dose groups as judged from 24 hour excretion profiles. Terminal distribution data showed no significant residual radioactivity in tissues 168 hours post-dose for both the low and high oral dose groups. Urine was the major route for excretion of diphenylamine derived radioactivity at both the low and high dose, with between 68-81% recovered for both sexes at the single and repeated low dose, and 73-74% recovered at the single high dose. Male rats appeared to excrete a greater percentage of diphenylamine derived radioactivity in urine at the low dose level, while female rats showed greater excretion in feces at this dose. At the high dose, the percentage eliminated in urine was equivalent in male and female rats.

Metabolites identified in urine in this study included dihydroxylated conjugates of diphenylamine, monohydroxylated sulfate conjugates of diphenylamine, and monohydroxylated glucuronide conjugates of diphenylamine. Male rats appeared to show a much greater percentage of dihydroxylated conjugates of diphenylamine in urine than female rats at both the single and repeated low oral dose, but not at the single high dose. In contrast, females showed higher urinary percentages of 4-hydroxydiphenylamine-O-sulfonic acid than males at all dose levels. Fecal metabolites consisted of the parent chemical and 4-hydroxydiphenylamine, which comprised only between 0.5-3% of the administered dose in both sexes (MRID 42994801).

Based on the available data for diphenylamine, the rat metabolism study with diphenylamine and the open literature data for diphenylamine and metabolites, there is no evidence that the N-nitroso metabolite of diphenylamine would be formed in rats or humans in vivo.

2. Dose Response Assessment

a. Reference Dose

The HED Reference Dose (RfD)/Peer Review Committee (document dated April 1, 1997) recommended that an RfD be established based on a chronic dog study with a LOEL of 10 mg/kg/day. An Uncertainty Factor (UF) of 100 was used to account for both the interspecies extrapolation and the intraspecies variability. An additional UF of 3 was recommended to account for the lack of a NOEL and the Committee's concern with respect to potential methemoglobinemia which was not tested in this study. On this basis, the RfD was calculated to be 0.03 mg/kg/day.

It should be noted that the LOEL was established at 10 mg/kg/day, in both males and females (based on hematological and clinical chemistry changes, and clinical signs of toxicity). Due to the lack of information on methemoglobinemia, the LOEL could not be verified and was considered tentative until this issue is addressed. The Agency recommended that a subchronic study of sufficient duration be conducted in dogs to investigate this possible methemoglobinemic effect to accurately define the NOEL in the critical study. The registrant is directed to contact the Agency before conducting such a study.

This chemical has been reviewed by the FAO/WHO joint committee meeting on pesticide residue (JMPR) and an acceptable daily intake (ADI) of 0.02 mg/kg/day has been established by that Committee.

b. Carcinogenicity Classification and Risk Quantification

The HED Reference Dose (RfD)/Peer Review Committee (document dated April 1, 1997) classified diphenylamine as "not likely" in reference to carcinogenicity. This classification was based on the lack of evidence for carcinogenicity in the two acceptable carcinogenicity studies in either male or female CD-1 mice or Sprague-Dawley rats.

c. Other Toxic Endpoints

The Agency's Health Effects Division's Toxicological Endpoint Selection Committee (document dated February, 27 1997) concluded the following for diphenylamine:

There are no dermal absorption data available; therefore, a default of 100% dermal absorption is assumed.

For acute dietary exposure (1 day) a risk assessment is not required since no appropriate endpoint or NOEL could be identified from the available data. No developmental toxicity was seen at doses greater than 100 mg/kg/day in rats or at doses greater than 300 mg/kg/day in rabbits.

For short term (1-7 day) or intermediate term (1 week to several months), **dermal** occupational:

In a 21 day dermal toxicity study, New Zealand White rabbits (5/sex/group) received repeated dermal applications (under occlusion) of diphenylamine Technical (100%) dissolved in distilled water at dose levels of 100, 500, or 1000 mg/kg for six hours a day for 21 consecutive days with terminal sacrifice on day 22. Two additional groups of rabbits of each sex (5/sex) served as the vehicle (distilled water) controls. None of the rabbits died, and with the exception of dark-red foci in the stomachs of both sexes at the 500 and 1000 mg/kg/day groups, the results of this study were unremarkable. The systemic toxicity NOEL was 100 mg/kg/day and the LOEL was 500 mg/kg/day based on the effects in the stomach. The dermal toxicity NOEL was greater than 1000 mg/kg/day (limit dose).

The dose and endpoint for use in risk assessment is the systemic NOEL of 100 mg/kg/day with a LOEL of 500 mg/kg/day based on dark-red foci in the stomachs of both sexes.

For chronic (several months to lifetime), **dermal** occupational exposures:

The dose and endpoint for use in risk assessment is the LOEL of < 10 mg/kg/day based on clinical chemistry observations based on a chronic dog study. An extra uncertainty factor of 3 is added to the usual uncertainty factor of 100 due to the lack of a NOEL in this study.

For **inhalation** (any duration) occupational exposures:

The requirement for an inhalation study was waived for the technical product. The formulation is placed in Toxicity Category III. A separate inhalation risk assessment is not required.

3. Exposure Assessment

This section describes the process the Agency used to estimate human exposure to diphenylamine from the diet and from occupational use.

a. Dietary Exposure

A dietary risk assessment is required when a chemical is registered for use on crops used either as food for people or feed for livestock. Diphenylamine

meets this criteria. Diphenylamine is a plant growth regulator currently registered in the U.S. for use on apples to prevent the appearance of the skin discoloration known as storage scald. Diphenylamine is formulated for post-harvest treatment on apples.

The residue chemistry data base identifying and quantifying the residues of diphenylamine is adequate and supports reregistration of diphenylamine as a food use pesticide on post-harvest treatment on apples. Tolerances are established for diphenylamine residues in apples (10 ppm), milk (0 ppm), and meat (0 ppm) [40 CFR §180.190]. No food or feed additive tolerances have been established for diphenylamine residues. The Agency has determined that the residue of concern in plants and livestock is diphenylamine *per se*.

Directions For Use

A search of the Agency's Reference Files System (REFS) on 12/19/96 identified two end-use products containing diphenylamine that are registered to members of the Diphenylamine Task Force. These end-use products, presented below, include an EC and an SC formulation.

Table 3: End Use Products

EPA Reg No.	Formulation	Label Date	Trade Name
2792-45	2.66 lb/gal EC	4/91[a]	No Scald DPA EC-283
64864-3	1.24 lb/gal SC/L	5/88	Shield Liquid DPA 15%

The 2.66 lb/gal EC can be applied post-harvest to apples as a dip, spray, or drench at concentrations of 1,000-2,200 ppm depending on apple variety, and the 1.2 lb/gal SC/L formulation can be applied post-harvest as a drench at the same concentrations. The labels specify that contact time with the treatment solution should not exceed 2 minutes and fruit should be thoroughly drained after treatment. Each 100 gal of treatment solution can treat 30 bins (500-750 bushels) of apples after which the treatment solution should be replaced. Labels indicate that fruit should be treated within 7 days after harvest prior to being placed in controlled atmosphere storage.

Nature of the Residue in Plants and Livestock

The qualitative nature of the residue in plants and livestock is adequately understood based on acceptable apple, ruminant and poultry metabolism studies. The Agency has concluded that the residue of concern in plants and livestock is diphenylamine, *per se* (C. Swartz, 2/10/95).

Residue Analytical Methods

Adequate analytical methods are available for data collection and tolerance enforcement in apples and apple processing fractions. A colorimetric method and

a GLC/electron capture detector (ECD) method are listed in PAM, Vol. II (Section 180.190) as Method I and Method B, respectively, for the quantitation of diphenylamine residues in apple commodities. Since Method I is a colorimetric method, it is no longer suitable as an enforcement method. However, a GC/mass selective detection (MSD) method for the quantitation of diphenylamine residues in apples and processed fractions has been submitted along with a successful independent method validation.

The GC/MSD method that was used to determine diphenylamine residues in milk and livestock tissues is adequate for data collection; however, an enforcement method must be provided. If the Task Force is proposing the GC/MSD method as an enforcement method, an independent laboratory method validation must be conducted as per PR Notice 96-1 (2/7/96).

Multiresidue Method Testing

The FDA PESTDATA database dated 1/94 (Pam Vol. I, Appendix I) indicates that diphenylamine is completely recovered using FDA Multiresidue Protocol D (PAM I Section 232.4) and that recovery of diphenylamine through FDA Multiresidue Protocol E (fatty and nonfatty, PAM I Sections 211.1 and 212.1) is low (< 50%).

Storage Stability Data

Adequate storage stability data are available to support the results of the magnitude of the residue studies in apples, apple processed fractions, meat and milk. Diphenylamine residues are stable at ≤-12° C for up to 155-167 days in apples and apple pomace (wet and dry) and for up to 202 days in apple juice. Diphenylamine residues are stable in frozen storage for up to 38 days in milk and muscle and for up to 54 days in liver.

Magnitude of the Residue in Crop Plants

Adequate magnitude of the residue data are available to support the use on apples. Acceptable residue data depicting diphenylamine residues in apples following a single post-treatment application at the maximum use rate have been submitted. These data indicate that the existing 10 ppm tolerance for diphenylamine residues in apples is appropriate.

Magnitude of the Residue in Processed Food/Feed

Adequate processing data are available to support the use on apples. Diphenylamine residues concentrated in wet pomace by a factor of 2.3-8.4X with an average of 4.7X. Residues did not concentrate in juice. Based on the highest

average field trial (HAFT) residue level of 5.86 ppm and the 4.7X average concentration factor for wet pomace, residues in wet pomace are estimated to be 27.5 ppm. Since the residues in wet pomace are expected to be 2.8X higher than the current 10 ppm tolerance for residues in apples, a 30 ppm tolerance for diphenylamine residues in wet apple pomace must be proposed.

Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

Adequate livestock feeding studies have been submitted to the Agency. The ruminant feeding study indicates the need for tolerances for diphenylamine in milk and animal commodities. A tolerance of 0.01 ppm is appropriate for residues in milk, and meat, fat, and meat by-products (excluding liver) of cattle, goats, horses, and sheep. The appropriate tolerance for diphenylamine residues in liver of these animals is 0.1 ppm.

Poultry and swine feeding studies are not required since there are no poultry or swine feed items associated with the use on apples, which is the only food/feed use currently being supported in the U.S.

Magnitude of the Residue in Water, Fish, and Irrigated Crops

Diphenylamine is not registered for direct use on potable water or aquatic food and feed crops; therefore, no residue chemistry data are required under these guideline topics.

Magnitude of the Residue in Food-Handling Establishments

Diphenylamine is not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

Confined Accumulation in Rotational Crops

Diphenylamine is not registered for use in the U.S. on any crops that are subject to rotation; therefore, no residue chemistry data are required under this guideline topic.

Field Accumulation in Rotational Crops

Diphenylamine is not registered for use in the U.S. on any rotated crops; therefore, no residue chemistry data are required under this guideline topic.

Dietary Exposure from Drinking Water

Diphenylamine was not included in the list of pesticides to be analyzed in well water/ground water in the Agency's Pesticides in Ground Water Database.

The Agency's EFED database and its "STORET" database were searched for monitoring data on diphenylamine residues in surface water. No data on diphenylamine residues in surface water are available.

Based on the limited use pattern for diphenylamine as a post-harvest drench on apples and the absence of detections in the ground water and surface water databases, dietary exposure from drinking water is expected to be negligible.

b. Occupational Exposure

An occupational exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete.

The Diphenylamine Task Force is only supporting the use in the prevention of storage scald on apples prior to entering storage. No other uses are assessed in this document. Application rates vary from 1,000 ppm to 2,200 ppm.

The registrant states that diphenylamine is applied to apples by a drive-through and an automated bin drencher. The DPA Task Force submitted a study on the two drenching process techniques for diphenylamine that were observed by an assessor. The registrant asserts that the drive-through drenching sites represents typical drenching operations. A typical description of the drive-through drenching process for diphenylamine is as follows:

"The drive-through drencher process involved a truck loaded with apple bins to pull into the drencher which is enclosed on the sides. The drencher is large enough for a flat bed truck with apple bins stacked up to 3 layers high to pull through. The truck cab is pulled beyond the application area before spraying begins. The driver stays in the cab during the process. Once the truck is inside the drencher, the operator turns on the spray nozzles from inside the drenching area and steps away from the application area. The truck driver pulls through slowly as the DPA material is applied to the apples using high-flow flood nozzles."

The assessor at the site observed that potential exposure could occur to handlers when diphenylamine is loaded into the tank. The highest potential exposure may occur from drift and over-spray from the drencher equipment onto the persons present during application and also from routine cleaning of the system.

Occupational-use products and homeowner-use products

At this time, products containing diphenylamine are intended for occupational use only and not for homeowner use.

Handler and Applicator Exposure

EPA has determined that there is a potential exposure scenario to the drencher operator during usual use-patterns associated with diphenylamine. Based on the use patterns, only one major exposure scenario was identified for diphenylamine drencher operator (the person outside of the the truck who turns on the spray nozzles).

Short-term and intermediate-term dermal exposures and risks (developed using PHED Version 1.1 surrogate data) are presented in Table 5 (page 25). No chemical-specific handler data were submitted. However, a surrogate PHED exposure assessment was submitted to the Agency (MRID 44212501). Table 4 (page 21) summarizes the caveats and parameters specific to the exposure scenario and corresponding risk assessment. No inhalation endpoints were identified; therefore an inhalation risk assessment was not required. A chronic endpoint using a LOEL of 10 mg/kg/day was identified. However, since no chronic exposure is expected (i.e., seasonal apple treatments), no chronic risk assessment was required.

The submitted surrogate assessment is limited to a mixer/loader PHED exposure estimate. The submission also presented site specific observations on the apple drenching process. These observations provided information on potential exposures. It was reported that exposure may result from adding diphenylamine to the tank and that the highest potential exposure may occur from the over-spray from the drencher equipment and perhaps routine cleaning of the system. EPA has modified this assessment to increase the number of observations in the mixer/loader assessment and to adjust for potential exposure during the over-spray from the drencher equipment. There are no known surrogate exposure data available for drencher operators. Therefore, EPA has developed a screening level assessment option to estimate potential exposure to a handler who both mixes/loads diphenylamine into the drencher equipment and operates the drencher equipment, and is potentially exposed to overspray. The option was developed by adding mixer/loader exposure to exposure of a flagger during aerial spray applications.

The following use information was supplied in the surrogate PHED submission:

Concentrations of diphenylamine in the spray solution range from 1,000 ppm to 2,200 ppm.

Number of apple bins treated per day ranges from 300 to 660.

An average of 50 gallons of spray solution is applied per bin.

EPA questions whether alternate methods of application are being used by some apple growers/processors. For example, whether the drench is sometimes applied during a conveyor belt operation. No data are available at this time concerning these potential exposures. The Agency does not expect the exposure for persons who may be handling the just treated apples and apple containers to be greater than the exposure to the drenchers.

Potential daily dermal exposure is calculated using the following formula:

DailyDermalExposure(mgai/day) =UnitExposure(mgai/lbai)xUseRate(lbai/gal)xDailyAmountTreated(gal/day)

No dermal absorption adjustment is necessary, since the endpoints are based on a dermal study.

These calculations of daily dermal exposure to diphenylamine by handlers are used to calculate the daily dose to those handlers.

Table 4: Exposure Scenario Descriptions for the Use of Diphenylamine

Exposure Scenario (Number)	Data Source	Standard Assumptions (8-hr work day)	Comments
Mixer/Loader/Applicator Descriptors			
Drencher Operator	PHED V1.1	Min.: 300 bins @ 50 gallons/bin Max.: 660 bins @ 50 gallons/bin	**Mixer/Loader Baseline:** "Best Available" grades: Hands and dermal = acceptable grades. Hands = 53 replicates; dermal = 25 to 122 replicates. High confidence in dermal data. **Mixer/Loader PPE:** "Best Available" grades: Hands and dermal = acceptable grades. Hands = 59 replicates; dermal = 25 to 122 replicates. High confidence in dermal data. **Applicator (Flagger) Baseline and PPE:** "Best Available" grades: Hands and dermal = acceptable grades. Hands = 16 replicates; dermal = 16 to 18 replicates. High confidence in dermal data. PHED data used for baseline, no Protection Factors (PFs) were necessary. A 50 percent PF was used to add a layer of coveralls for the mixer/loader and applicator PPE scenarios.

[a]Standard Assumptions based on an 8-hour work day as estimated by the Agency. Other data were not available.
[b]"Best Available" grades are defined by the Agency's SOP for meeting Subdivision U Guidelines. Best available grades are assigned as follows: matrices with grades A and B data and a minimum of 15 replicates; if not available, then grades A, B and C data and a minimum of 15 replicates; if not available, then all data regardless of the quality and number of replicates. Data confidence are assigned as follows:

High = grades A and B and 15 or more replicates per body part
Medium = grades A, B, and C and 15 or more replicates per body part
Low = grades A, B, C, D and E or any combination of grades with less than 15 replicates

Post Application Exposure

At this time, EPA is not concerned about post-application exposures to treated apples and apple containers. Available information show that post-

application handling of the apples and apple bins are done by forklift machinery thereby minimizing, if not eliminating, possible worker exposure.

4. Risk Characterization

a. Dietary Risk

(1) Acute Dietary Risk

A risk assessment was not conducted for acute dietary exposure since no appropriate endpoint or NOEL could be identified from the available data. No developmental toxicity was seen at doses greater than 100 mg/kg/day in rats or at doses greater than 300 mg/kg/day in rabbits.

(2) Chronic and Carcinogenic Dietary Risk

An RfD is used to assess the dietary cancer risk for a chemical. The chronic dog feeding study for diphenylamine was used to calculate the RfD. Systemic toxicity was noted at the lowest dose tested (10 mg/kg/day). Uncertainty factors of 10 each for both intra- and inter- species variability were applied as well as an additional factor of 3 to account for the lack of a NOEL. The RfD was calculated to be 0.03 mg/kg/day.

A Dietary Risk Evaluation System (DRES) chronic exposure analysis was performed using tolerance level residues and 100 percent crop treated information to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. The TMRC for the U.S. population utilized 32.12% of the RfD and 324.68% of the RfD for non-nursing infants (< 1 year old). Anticipated residue data were used to calculate the Anticipated Residue Concentration (ARC) for those same population subgroups for certain commodities in order to refine the dietary risk assesment. The ARC for existing tolerances utilizes 2% of the RfD for the general U.S. population and 20.1% of the RfD for non-nursing infants (< 1 year old). Adding exposures from meat and milk which currently have tolerances at 0 ppm results in an ARC of 2.27% of the RfD for the general U.S. population and 20.8% of the RfD for non-nursing infants (< 1 year old). Since all chronic risk falls below 100% of the RfD, there is no chronic dietary risk concern for diphenylamine.

Diphenylamine is classified as "not likely" to be carcinogenic to humans based on the lack of evidence for carcinogenicity in two studies. However, diphenylnitrosamine, an impurity of technical grade diphenylamine has been classified as a probable human carcinogen based on increased incidence of bladder tumors in male and female rats, reticulum cell sarcomas in mice and structural relationship to carcinogenic nitrosamines.

A dietary risk assessment for diphenylnitrosamine, was conducted to determine the cancer risk from exposure to the impurity. The nitrosamine level of 10 ppm (0.00001) was multiplied by the ARC (0.000568 mg/kg/day) to obtain the level of exposure. This was then multiplied by the Q_1* or cancer potency of 4.9 X 10^{-3} mg/kg/day, as reported on IRIS for nitrosamines, to obtain the cancer risk of 2.8 X 10^{-11} mg/kg/day. The chronic DRES analysis calculated an anticipated residue contribution (ARC) for the total U.S. Population of 0.000568 mg/kg/day.

To calculate the cancer risk for the nitrosamine, the Agency multiplied the ARC (0.000568 mg/kg/day) by 10^{-5} (because diphenylnitrosamine is 10 ppm or 10/1,000,000). This result was multiplied by the Q_1* of 0.0049 mg/kg/day and the lifetime (70 years) cancer risk was calculated to be 2.8 x 10^{-11}.

$0.000568 \text{ mg/kg/day} \times 10^{-5} = 5.6 \times 10^{-9}$

$5.6 \times 10^{-9} \times 4.9 \times 10^{-3} = 2.8 \times 10^{-11}$ mg/kg/day

This value is well below the Agency's level of concern of 1 x 10^{-6} for nitrosamine in the diet .

(3) Drinking Water Risk

Based on the absence of detections in the Agency's Pesticides in Ground Water Database or in the U.S. EPA's "STORET" database, and the limited use pattern, dietary risk from drinking water is assumed to be negligible.

b. Occupational and Residential Risk Characterization

Risk Estimates For Handler Exposures

Dermal

The daily dermal dose is calculated using a 70 kg body weight for short-term exposure and a 70 kg body weight for intermediate-term exposure.

$$\text{Daily Dermal Dose}\left(\frac{\text{mg ai}}{\text{Kg/Day}}\right) = \text{Daily Dermal Exposure}\left(\frac{\text{mg ai}}{\text{Day}}\right) \times \left(\frac{1}{\text{Body Weight (Kg)}}\right)$$

These calculations of daily dermal dose of diphenylamine received by handlers are used to assess the dermal risk to those handlers. The short-term dermal MOEs were calculated using a NOEL of 100 mg/kg/day. The short-term and intermediate-term dermal MOEs were calculated using a NOEL of 100 mg/kg/day in the following formula:

$$MOE = \frac{NOEL\left(\frac{mg}{kg/day}\right)}{Daily\ Dermal\ Dose\left(\frac{mg}{kg/day}\right)}$$

Dermal Risk from Handler Exposures

Short-term and Intermediate-term

The calculations of short-term and intermediate-term dermal risk indicate that the MOEs are more than 100 at **baseline** (i.e. clothing worn include long pants, long sleeved shirt and no gloves for the exposure scenario combining open mixing/loading and flagger) for the following scenarios:

- None for either minimum or maximum concentrations.

Table 5: Short-term and Intermediate-term Dermal Exposures and Risks to Diphenylamine

Exposure Scenario	Baseline Dermal Unit Exposure (mg/lb ai)[a]	Application Rate (lb ai/gallon)[b]	Daily Gallons Used[c]	Amount of ai Handled per Day (lb ai)	Daily Dermal Exposure (mg/day)[d]	Baseline Dermal Dose (mg/kg/day)[e]	Baseline Dermal MOE[f]	Risk Mitigation Measures Additional PPE		
								Dermal Unit Exp. (mg/lb ai)[g]	PPE Dermal Dose (mg/kg/day)[e]	PPE Dermal MOE[f]
Mixer/Loader/Applicator Exposure/Risk										
Drench operator	Flagger scenario: 2.91	Min. 0.0081	15,000	121.5	354	5.1	20	0.05	0.09	1,111
		Max. 0.0181	33,000	597.3	1,738	24.8	4		0.43	233

[a] Baseline dermal unit exposure represents a combination of open mixing/loading liquid formulations (unit exposure = 2.9 mg/lb ai) the exposure of a flagger (unit exposure = 0.01 mg/lb ai). Clothing worn includes long pants, long sleeved shirt, and no gloves.
[b] Spray solution concentrations are based on the label's minimum (Min. = 1,000 ppm) and the maximum (Max. = 2,200 ppm) concentrations. Assessments have been calculated for both the minimum and maximum concentrations.
[c] The registrant reported a range of treatments per day as (Min.) 300 bins to (Max.) 660 bins with an average of 50 gallons per bin.
[d] Daily dermal exposure (mg/day) = Exposure (mg/lb ai) * Appl. rate (lb ai/gallon) * Gallons treated.
[e] Dermal Dose (mg/kg/day) = Dermal Exposure (mg/day) / Body Weight (70 kg).
[f] Dermal MOE = NOEL (100 mg/kg/day) / Daily Dermal Dose (mg/kg/day).
[g] PPE dermal unit exposure represents a combination of open mixing/loading liquid formulations and the exposure of a flagger. For the minimum and maximum application rate, the PPE scenario is single layer body covering and chemical-resistant gloves for the mixing/loading portion of the operation and single layer body protection with no gloves during the application operation (unit exposure = 0.043 mg/lb ai for the mixer/loader and 0.007 mg/lb ai for flaggers).

The calculations of short-term and intermediate-term dermal risk indicate that the MOEs are more than 100 with **additional PPE** (single layer body covering and chemical-resistant gloves for mixing/loading and single layer body covering with no gloves during application)for the following scenarios:

- minimum and maximum concentrations and minimum and maximum amounts handled for the drencher operator.

The calculations of short-term and intermediate-term dermal risk indicate that the MOEs are not more than 100 despite the maximum mitigation measure for the following scenario:

- none

Dermal Risk - Diphenylnitrosamine

A worker risk assessment for nitrosamine, an impurity in technical grade diphenylamine was calculated using the following assumptions. The product contains 10 ppm of the impurity, a worker has 90 days of exposure per year and a 35 year work life. Dermal absorption is assumed to be 100% and the Q_1* is 0.0049 mg/kg\day. The worker risk range from 5.4×10^{-10} to 1.3×10^{8} . The worker risk from nitrosamine is below the Agency's level of concern

Additional Occupational Exposure Studies

Handler Studies

EPA is requiring the registrant to conduct a deposition study. The results will be used to determine the need for additional dermal exposure studies for this application scenario. These data are considered confirmatory. In addition, EPA is requiring the registrant to submit more documentation regarding alternative methods of drenching, particularly the automated bin drenching system and conveyor belt drenching operations.

Post-Application Studies

There are no post-application studies required at this time since available information show that handling of apples, apple containers, and other items wet with diphenylamine to be tasks performed by forklift machinery, thereby minimizing, if not eliminating, post-application worker exposure.

5. FQPA Considerations

The Food Quality Protection Act of 1996 (FQPA) amended the FFDCA by setting a new safety standard for the establishment of tolerances. In determining whether a tolerance meets the new safety standard, section 408(b)(2)(C) directs EPA to consider information concerning the susceptability of infants and children to pesticide residues in food, and available information concerning aggregate exposure to infants and children of such residues, as well as the potential for cumulative effects from pesticide residues and other substances that have a common mechanism of toxicity.

The FQPA amendments to section 408(b)(2)(C) require EPA to apply an additional 10-fold uncertainty (safety) factor unless reliable data demonstrate that the additional factor is unnecessary to protect infants and children.

Section 408(b)(2)(D) establishes factors that the Agency must consider in determining whether the safety standard is met in deciding to issue or reassess tolerances. These factors include the consideration of available information on the aggregate exposures to the pesticide from dietary sources including drinking water as well as non-occupational exposures such as those derived from pesticides used in and around the home. The Agency must also consider the potential cumulative effects of the pesticide for which a tolerance is being sought as well as other substances that have a common mechanism of toxicity.

Because diphenylamine has food uses, specific consideration of the risks to infants and children, as well as aggregate exposures and potential cumulative effects is warranted.

Potential Risk to Infants and Children

In determining whether an additional uncertainty factor is or is not appropriate for assessing risks to infants and children, EPA uses a weight of evidence approach taking into account the completeness and adequacy of the toxicity data base, the nature and severity of the effects observed in pre- and post-natal studies, and other information such as epidemiological data.

For purposes of assessing the pre- and post-natal toxicity of diphenylamine, EPA has evaluated two developmental and one reproduction study. Based on current toxicological data requirements, the data base for diphenylamine, relative to pre- and post-natal toxicity, is complete. However, as EPA fully implements the requirements of FQPA, additional data related to the special sensitivity of infants and children may be required.

The data provided no indication of increased sensitivity of rats or rabbits to *in utero* and/or post-natal exposure to diphenylamine. The reproduction study demonstrated that the offspring were less sensitive than the adults and there was no developmental toxicity observed in either the rat or rabbit developmental studies at any dose tested.

Uncertainty Factor

Based on the considerations outlined above, the Agency concludes that an additional uncertainty factor to account for any special sensitivity to infants and children is not warranted for diphenylamine or the impurity nitrosamine.

Aggregate Exposure

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and

other exposures for which there is reliable information. These other exposures include drinking water and non-occupational exposures, e.g., to pesticides used in and around the home. Risk assessments for aggregate exposure consider both short-term and long-term (chronic) exposure scenarios including the toxic effects which would likely be seen for each exposure duration.

Since there are no data on diphenylamine in the Agency's Pesticides in Ground Water Database or in the U.S. EPA's "STORET" database, and the limited use pattern, dietary risk from drinking water will assumed to be negligible. Diphenylamine is a food use chemical. There are no residential (non-occupational) uses of diphenylamine; therefore the considerations for aggregate exposure are those only from food.

Acute Risk

As previously discussed, an acute dietary risk assessment was not conducted since no appropriate endpoint or NOEL was identified in the available studies.

Chronic Risk

The chronic dietary risk evaluation indicated that exposure to diphenylamine through food containing residues of this pesticide are below the Agency's level of concern (i.e., the percent RfD utilized is only 20.8 percent for non-nursing infants, the most sensitive subpopulation).

Cumulative Exposure To Substances with Common Mechanism of Toxicity.

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and

evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical specific data, much of which may not be presently available.

Although at present, the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

EPA does not have, at this time, available data to determine whether diphenylamine has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, EPA has not assumed that diphenylamine has a common mechanism of toxicity with other substances.

C. Environmental Assessment

1. Ecological Toxicity Data

Diphenylamine is moderately toxic to fish and aquatic invertebrates. It is practically non-toxic to avian species on an acute and subacute basis. Since this is an indoor food use chemical, and given the the limited volume and pattern of DPA use, the likelihood of adverse effects on ecological systems is considered to be minimal. No further data are required. Discharge of effluent containing diphenylamine for manufacturing use is regulated by NPDES.

a. Toxicity to Terrestrial Animals

Only acute oral and subacute dietary studies are required for birds due to the indoor-food end-use pattern. The results are discussed below.

(1) Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of diphenylamine to birds. The preferred test species is either mallard duck (a waterfowl) or bobwhite quail (an upland gamebird). The result of this test is tabulated below.

Table 6: Avian Acute Oral Toxicity

Species	% ai	LD_{50} (mg/kg)	Toxicity Category	MRID No. Author/Year	Study Classification[1]
Northern bobwhite quail *(Colinus virginianus)*	100	> 2250	Practically nontoxic	43878901 Palmer/Beavers 1995	Core

[1] Core (study satisfies guideline). Supplemental (study is scientifically sound, but does not satisfy guideline)

Since the LD50 is greater than 2250 mg/kg, diphenylamine is categorized as practically non-toxic to avian species on an acute oral basis. Guideline 71-1 is fulfilled (MRID 4387901).

A sub-acute dietary study using the TGAI is required to establish the toxicity of diphenylamine to birds for the indoor-food end-use. The preferred test species is either mallard duck or bobwhite quail. The result of this test is tabulated below.

Table 7: Avian Subacute Dietary Toxicity

Species	% ai	5-Day LC_{50} (ppm)[1]	Toxicity Category	MRID No. Author/Year	Study Classification
Mallard duck *(Anas platyrhynchos)*	100	> 5205	Practically non-toxic	43879101 Palmer/Beavers 1995	Core

[1] Test organisms observed an additional three days while on untreated feed.

Since the LC50 is greater than 5205 ppm, diphenylamine is categorized as practically non-toxic to avian species on a subacute dietary basis. Guideline (71-2) is fulfilled (MRID 43879101).

(2) Birds, Chronic

Avian reproduction studies using the TGAI are not required for diphenylamine because of the intended indoor-food end-use.

(3) Mammals, Acute and Chronic

Wild mammal studies using the TGAI are not required for diphenylamine because of the intended indoor-food end-use.

(4) Insects

A honey bee acute contact study using the TGAI is not required for diphenylamine because its use will not result in honey bee exposure.

b. Toxicity to Aquatic Animals

Only acute studies are required for fish and aquatic invertebrates because of the indoor-food end-use. The results are presented below:

(1) Freshwater Fish, Acute

One freshwater fish toxicity study using the TGAI is required to establish the toxicity of diphenylamine to fish for the indoor-food end-use. The preferred test species is either rainbow trout (a coldwater fish) or bluegill sunfish (a warmwater fish). The result of this test is tabulated below.

Table 8: Freshwater Fish Acute Toxicity

Species/ Flow-through or Static	% ai	96-hour LC_{50} (ppm) (measured/nominal)	Toxicity Category	MRID No. Author/Year	Study Classification
Rainbow trout *(Oncorhynchus mykiss)* static	100	2.2 (measured)	Moderately toxic	43879001 Drottar/Swigert 1995	Core

Since the LC_{50} is 2.2 ppm, diphenylamine is categorized as moderately toxic to freshwater fish on an acute basis. Guideline 72-1 is fulfilled (MRID 43879001).

(2) Freshwater Fish, Chronic

A freshwater fish early life-stage test using the TGAI is not required for diphenylamine because of the intended indoor-food end-use, and its relative low acute toxicity.

(3) Freshwater Invertebrates, Acute

A freshwater aquatic invertebrate toxicity test using the TGAI was required to establish the toxicity of diphenylamine to aquatic invertebrates. The preferred test species is *Daphnia magna*. The result of this test is tabulated below.

Table 9: Freshwater Invertebrate Acute Toxicity

Species/Static or Flow-through	%ai	48-hour LC_{50}/EC_{50} (ppm) (measured)	Toxicity Category	MRID No. Author/Year	Study Classification
Waterflea *(Daphnia magna)*	100	1.2	Moderately toxic	43878301 Drottar/Swigert 1995	Core

Since the EC_{50} is 1.2 ppm, diphenylamine is categorized as moderately toxic to aquatic invertebrates on an acute basis. Guideline 72-2 is fulfilled (MRID 43878301).

(4) Freshwater Invertebrate, Chronic

A freshwater aquatic invertebrate life-cycle test using the TGAI is not required for diphenylamine because of the intended indoor-food end-use.

2. Environmental Fate Characteristics of Diphenylamine Summary

Since this is an indoor-food end-use chemical, only hydrolysis data are required. The available data indicate that diphenylamine is stable towards hydrolysis at pH's 5, 7, and 9. Based on limited laboratory data only, the Agency concludes:

Diphenylamine has a moderate solubility in water (39.4 ppm), a relatively high octanol/water partition coefficient ($K_{OW} = 3{,}860$), and a high vapor pressure (6.39×10^{-4} torr).

Diphenylamine appears to be very labile in the environment, with aerobic soil metabolism, and aqueous photolysis having important roles in the dissipation of the molecule. Under aerobic soil metabolism conditions, diphenylamine is rapidly transformed to dimers and polymers (half-life < 1 day). In addition, when exposed to light in aqueous media, transformation is rapid (half-life 4.39 hours).

There is relatively little information about the transformation products formed when diphenylamine is subjected to aerobic soil metabolism or aqueous photolytic conditions. As mentioned earlier many of the ultimate transformation products of diphenylamine are dimers and polymers with structures more complex than that of diphenylamine. The rate of dissipation of such compounds is unknown although it appears that they are much more stable than parent diphenylamine.In aerobic soils it appears that the ultimate fate of the diphenylamine residues is mineralization (formation of CO_2; 17.87% of the applied after 365 days), and soil binding (unextracted residues 57.89% of the applied at 184 days).

The mobility of diphenylamine ranges from somewhat mobile ($K_{ads} = 151.57$ in clay soil), to mobile ($K_{ads} = 21.43$ for loamy sand, $K_{ads} = 13.79$ for loam, $K_{ads} = 4.92$ for silt loam, and $K_{ads} = 16.44$ for silty clay loam). Diphenylamine residues (parent diphenylamine aged under aerobic soil metabolism conditions for 16.5-24.5 hours) were mobile in silt loam soil columns, and slightly mobile in loamy sand, loam and clay soil columns.

Because this chemical is used indoors only, it is highly unlikely that it will runoff to surface waters. However, if used outdoors there is a potential to reach surface waters via dissolved runoff events occurring immediately after application. The high rate of aqueous photolysis and the susceptibility of the chemical in aerobic environments indicate that if it were to reach surface waters, however, the chemical would be short lived.

Hydrolysis

[^{14}C]-Diphenylamine (uniformly ring-labeled), at about 7 ppm, was relatively stable towards hydrolysis in pH 5, 7, and 9 buffered aqueous solutions at $25 \pm 1\,^{\circ}C$. The registrant-calculated half-lives ranged from 316 to 358 days.

Four minor degradates (≤3.08% of the applied radioactivity) were detected in all buffer solutions, but not identified. This study is acceptable and can be used to satisfy the Hydrolysis data requirement. No additional data are required. (MRID 42660001)

The following studies are not required to satisfy the current data requirements for diphenylamine; however, EFED reviewed the studies and included the information in the chemical's database:

Photodegradation in Water

[U-^{14}C]Diphenylamine, at 5 ppm, photolyzed with a registrant-calculated half-life of 4.39 hours in a sterile aqueous pH 7 buffer solution that was irradiated with a xenon lamp at 25°C for 192 hours. The major transformation products observed were as follows:

Carbazole (D1), reached a maximum of 51.74% of the applied at 10.5 hours, and decreased to non-detectable levels from 72 to 192 hours.

Hydroxydiphenylamine (OH-DPA, D2), averaged a maximum of 16.34% of the applied at 36 hours and decreased to 6.83% by 192 hours.

A hydroxylated tricyclic compound (D3), was first detected at 4 hours(< 1% of the applied) and increased gradually to 93.18% at 192 hours (last test interval).

Three other minor transformation products were observed, at ≤ 5.87% of the applied.

This study is acceptable and can be used to satisfy a Photolysis in Water (guideline 161-2) data requirement. No additional data are required. (MRID 42958201)

Aerobic Soil Metabolism

[U-^{14}C]Diphenylamine, at 10 ppm, dissipated with an observed half-life of < 1 day in loam soil that was incubated in the dark at 24-26°C and 75% field moisture capacity. Twelve [^{14}C] compounds were isolated (≤18.9% of the applied) from the soil but could not be identified. Such compounds were characterized as polymers, most of which contained dimeric diphenylamine with one additional unit of aniline.

[$^{14}CO_2$] averaged 17.87% of the applied by 365 days post-treatment. Unextracted [^{14}C] residues increased to ≥46.40% of the applied by 3 days post-treatment and thereafter (maximum of 57.89% at 184 days).

This study is acceptable and can be used to satisfy an Aerobic Soil Metabolism (162-1) data requirement. No additional data are required. (MRID 42964201)

Anaerobic Aquatic Metabolism

This study is unacceptable, but does not have to be repeated. It cannot be used to satisfy any data requirements for the following reasons:

- A number of samples (not identified by the registrant) appear to have become aerobic during the study. This change confounded the analysis of the information provided.

- The [^{14}C] in the acetonitrile:methylene chloride extracts were assumed to contain only the parent diphenylamines while the TLC analyses of the same extracts showed the presence of various components. These components were neither identified nor quantified.

[U-^{14}C]Diphenylamine, at about 10 ppm, appears to dissipate slowly, with a registrant calculated half-life of 60 days in anaerobic silty clay loam sediment (flooded plus nitrogen atmosphere) incubated in the dark at 25°C for up to 1 year. $^{14}CO_2$ was ≤3.13% of the applied throughout the study. Unextracted [^{14}C] residues were 23.13-44.22% of the applied at 364 days. Up to 69.91% of the applied radioactivity was volatilized and found in the rubber stoppers. (MRID 43080901)

Mobility-Leaching and Adsorption/Desorption

Based on batch equilibrium experiments, [U-^{14}C]diphenylamine, at approximately 0.10, 1.0, 5.0, and 10.0 µg/mL, was mobile in loamy sand soil, loam soil, silt loam soil, and silty clay loam sediments, and somewhat mobile in clay soil. Freundlich K values were as follows:

Table 10: Freundlich K values for Diphenylamine

Soil type	K_{ads}	K_{oc}	K_{des}
loamy sand	21.43	3622	34.67
loam	13.79	3962	23.51
silt loam	4.92	1212	8.73
silty clay loam sediment	16.44	6593	39.58
clay	151.57	5143	306.56

This study is acceptable and can be used to partially satisfy a Mobility-Leaching and Adsorption/Desorption (163-1) data requirement by providing information about the mobility of unaged diphenylamine. No additional data are required. (MRID 43412701)

Mobility-Leaching and Adsorption/Desorption

Based on column leaching studies, unaged [^{14}C]diphenylamine was relatively mobile in columns of silt loam and loamy sand soil. It was somewhat mobile in columns of loam soil and relatively immobile in columns of clay soil. All columns were treated with about 500μg of [^{14}C]diphenylamine and leached with 20 inches of 0.01 M calcium chloride solution.

In the loamy sand, an average of 37.5% of the applied was found in the treated soil layer. In the first two segments 61.66% was observed and in segments 3-5 ≤0.16% was observed. The leachate contained only 0.11% of the applied. In the silt loam soil 23.71 - 27.26% of the applied was found in segments 1, 2, and the treated soil layer. 6.07% was found in segment 3, and ≤1.88% was found in the leachates and segments 4 and 5. In the loam soil columns, the majority of the radioactivity was in the treated segment, with 75.12% of the applied, followed by segments 1 and 2, with 15.54% and 2.54%, respectively. Segments 3-5 and the leachate contained ≤0.48% of the applied. In the clay soil, 88.77% of the applied was in the treated segment, and ≤0.15% was observed in the other segments and the leachate.

Based on column leaching experiments, [^{14}C]diphenylamine residues were mobile in silt loam soil columns, slightly mobile in loamy sand, loam and clay soil columns. Prior to leaching, each column was topped with 50 g of soil that had been treated with [U-^{14}C] diphenylamine and incubated for 16.5-24.5 hours.

The loam, loamy sand, and clay soils had a similar radioactivity profile, with 85.43-108.21% of the applied in the aged soil layer, 3.84-7.32% of the applied in the first segment, 0.79-1.83% in the second segment, ≤ 0.35% in segments 3 to 5, and ≤1.06% in the leachate fractions. In the silt loam only, an average of 35.62% of the applied radioactivity was in the aged soil, 17.40% was in segment 1, 27.73% was in segment 2, 10.47% in segment 3, 1.57% in segment 4, 0.74% in segment 5, and 4.19% of the applied in the leachate.

In the soil columns, the following transformation products were observed:

N,N-Diphenylformamide (DPF),
4-nitro-N-phenylbenzenamine (NDPA),
diphenylamine dimer 1 (DPA-1), and
diphenylamine dimer 2 (DPA-2).

This study is acceptable and can be used to partially satisfy a Mobility-Leaching and Adsorption/Desorption (163-1) data requirement by providing information about the mobility of aged diphenylamine. No additional data are required. (MRID 43413001)

3. Exposure and Risk Characterization

Diphenylamine is moderately toxic to fish and aquatic invertebrates. It is practically non-toxic to avian species on an acute and subacute basis. This is an indoor food use chemical, and discharge of effluent containing diphenylamine for manufacturing use is regulated by NPDES permit. EFED does not conduct risk assessments for indoor use chemicals. However, given the limited volume and pattern of diphenylamine use, the likelihood of adverse effects on ecological systems is considered to be minimal.

4. Endangered Species

Because of minimal expected adverse risk on ecological systems due to the unlikeliness of exposure, the usual statement concerning endangered species is not necessary for diphenylamine.

5. Labelling

The "Environmental Hazards" section should include the following:

Manufacturing Use

"This pesticide is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewage systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."

End-Use Product

"This pesticide is toxic to fish and aquatic invertebrates. Do not contaminate water by cleaning of equipment or disposing of equipment washwater or rinsate."

6. Data Requirements

All ecological toxicity and environmental fate data requirements for diphenylamine are fulfilled.

IV. RISK MANAGEMENT AND REREGISTRATION DECISION

A. Determination of Eligibility

Section 4(g)(2)(A) of FIFRA calls for the Agency to determine, after submission of relevant data concerning an active ingredient, whether products containing the active ingredients are eligible for reregistration. The Agency has previously identified and required the submission of the generic (i.e. active ingredient specific) data required to support reregistration of products containing diphenylamine as active ingredients. The Agency has completed its review of these generic data, and has determined that the data are sufficient to support reregistration of all products containing diphenylamine. Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of diphenylamine, and lists the submitted studies that the Agency found acceptable.

The data identified in Appendix B were sufficient to allow the Agency to assess the registered uses of diphenylamine and to determine that diphenylamine can be used without resulting in unreasonable adverse effects to humans and the environment. The Agency therefore finds that all products containing diphenylamine as the active ingredients are eligible for reregistration. The reregistration of particular products is addressed in Section V of this document.

The Agency made its reregistration eligibility determination based upon the target data base required for reregistration, the current guidelines for conducting acceptable studies to generate such data, published scientific literature, etc. and the data identified in Appendix B. Although the Agency has found that all uses of diphenylamine are eligible for reregistration, it should be understood that the Agency may take appropriate regulatory action, and/or require the submission of additional data to support the registration of products containing diphenylamine, if new information comes to the Agency's attention or if the data requirements for registration (or the guidelines for generating such data) change.

B. Determination of Eligibility Decision

1. Eligibility Decision

Based on the reviews of the generic data for the active ingredients diphenylamine, the Agency has sufficient information on the health effects of diphenylamine and on its potential for causing adverse effects in fish and wildlife and the environment. The Agency has determined that diphenylamine products, labeled and used as specified in this Reregistration Eligibility Decision, will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, the Agency concludes that products containing diphenylamine for all uses are eligible for reregistration.

2. Eligible and Ineligible Uses

The Agency has determined that the currently registered use of diphenylamine is eligible for reregistration subject to conditions imposed in this RED.

C. Regulatory Position

The following is a summary of the regulatory positions and rationales for diphenylamine. Where labeling revisions are imposed, specific language is set forth in Section V of this document.

1. FQPA Findings

Because diphenylamine has a food use, specific consideration of the risks to infants and children, as well as aggregate exposures and potential cumulative effects, is warranted.

In determining whether an additional uncertainty factor is or is not appropriate for assessing risks to infants and children, EPA uses a weight of evidence approach taking into account the completeness and adequacy of the toxicity data base, the nature and severity of the effects observed in pre- and post-natal studies, and other information such as epidemiological data.

For purposes of assessing the pre- and post-natal toxicity of diphenylamine, EPA has evaluated two developmental and one reproduction study. Based on current toxicological data requirements, the data base for diphenylamine, relative to pre- and post-natal toxicity, is complete. However, as EPA fully implements the requirements of FQPA, additional data related to the special sensitivity of infants and children may be required.

The data provided no indication of increased sensitivity of rats or rabbits to *in utero* and/or post-natal exposure to diphenylamine. The reproduction study demonstrated that the offspring were less sensitive than the adults and there was no developmental toxicity observed in either the rat or rabbit developmental studies at any dose tested.

Based on the considerations outlined above, the Agency concludes that an additional uncertainty factor to account for any special sensitivity to infants and children is not warranted for diphenylamine.

There are no data or information to indicate that diphenylamine will contaminate drinking water. Additionally, it is unlikely for this to occur given the limited use pattern for this chemical. There are also no residential uses for diphenylamine. Therefore, aggregate exposure is obtained only from the use on apples.

It is not appropriate to conduct an acute dietary risk assessment as no acute endpoint or NOEL was identified in the available studies.

The chronic dietarty risk assessment using anticipated residues for some commodities indicated that only 20.8 percent of the RfD is utilized for the most sensitive subpopulation, non-nursing infants.

A dietary cancer risk asesment for the impurity diphenylnitrosamine was also conducted and indicated that the estimated lifetime cancer risk is 2.8×10^{-11}.

Both the non-cancer and cancer dietary risk assessments indicate that the risk fall below the Agency's levels of concern.

EPA does not have, at this time, available data to determine whether diphenylamine has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, EPA has not assumed that diphenylamine has a common mechanism of toxicity with other substances.

2. Tolerance Reassessment

A summary of the diphenylamine tolerance reassessment and recommended modifications in commodity definitions are presented in Table 11.

Tolerances Listed Under 40 CFR §180.190:

Adequate residue data are available to determine the adequacy of the established tolerances on apples, milk, and meat. The residue data support the current tolerance of 10 ppm for residues in apples. Data indicate that tolerances for residues in milk and meat, both currently 0 ppm, should be increased. Separate tolerances of 0.01 ppm should be established for residues in milk and meat, fat, and mbyp (excluding liver) of cattle, goats, horses, and sheep. Separate tolerances of 0.1 ppm should be established for residues in liver of cattle, goats, horses, and sheep.

New Tolerances Needed Under 40 CFR §180.190:

Data from an adequate apple processing study indicate that the registrants should propose a tolerance of 30 ppm for diphenylamine residues in wet apple pomace.

Table 11: Tolerance Reassessment Summary for Diphenylamine.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR §180.190:			
Apples	10.0	10.0	
Milk	0	0.01	Data from the ruminant study indicate that a higher tolerance is required.
Meat	0	0.01	Residue data from a ruminant feeding study indicate that a higher tolerance is required. Separate tolerances must be established for *meat, fat, and mbyp (excluding liver) of cattle, goats, horses, and sheep*.
Tolerances needed under 40 CFR §180.190:			
Liver	None	0.1	Residue data from a ruminant feeding study indicate a tolerance is required. Separate tolerances must be established for *liver of cattle, goats, horses, and sheep*.
Apple, pomace, wet	None	30.0	Residue data from an apple processing study indicate that a tolerance for residues in wet apple pomace is required.

Dietary Exposure Assessment Summary

Adequate plant and livestock metabolism and residue data are available for reregistration and risk assessment. Although additional data are required for the livestock enforcement method, a risk assessment can be performed at this time. The residue levels to be used in the risk assessment are shown in the tolerance reassessment summary.

Codex Harmonization

The Codex Alimentarius Commission has established a maximum residue limit (MRL) for diphenylamine residues in apples (see *Guide to Codex Maximum Limits For Pesticide Residues, Part A.1-58, 1995*). The Codex residue definition and the U.S. tolerance expression for diphenylamine are currently compatible, since each includes only the parent, diphenylamine. However, the Codex MRL (CXL) for diphenylamine on apples is 5 mg/kg compared to the 10 ppm U.S. tolerance for apples. Since available residue data, based on the current U.S. use pattern, indicate that the 10 ppm tolerance is appropriate, harmonization of the Codex MRL and U.S. tolerance is not possible at the present time.

3. Tolerance Revocations and Import Tolerances

At this time EPA, does not have any issues or recommendations for diphenylamine relative to tolerance revocations or import tolerances.

4. Summary of Risk Management Decisions

a. Human Health

(1) Dietary

Acute Dietary

An acute dietary risk assessment was not conducted since no appropriate endpoint or NOEL could be identified from the available data. No developmental toxicity was seen at doses greater than 100 mg/kg/day in rats or at doses greater than 300 mg/kg/day in rabbits.

Chronic Dietary (including cancer)

The Agency has evaluated the chronic dietary risk associated with consuming food containing residues of diphenylamine. Anticipated residues for some commodities were used to estimate exposure. The RfD was determined to be 0.03 mg/kg/day based on the LOEL observed in a chronic dog feeding study and uncertainty factors of 10 for both intra- and inter species variability and 3 for the lack of a NOEL. The percent RfD utilized for the most sensitive subpopulation (non-nursing infants) was calculated to be 20.8 percent; well below the Agency's level of concern.

No dietary cancer risk assessment was performed for diphenylamine since available data indicate it is not carcinogenic. However, an impurity, diphenylnitrosamine, has been determined to be carcinogenic and the dietary risk is calculated to be 2.8×10^{-11} for a lifetime of exposure. This level of risk is considered to be negligible and not of concern.

(2) Worker (Mixer/Loader/Applicator)

Acute (Short-Term) and Intermediate Term

EPA has determined that there is potential exposure to pesticide handlers from the use of diphenylamine as a drench on apples following harvest.

Exposure data for this use pattern are not available; consequently, the Agency had to rely on surrogate data and adjust to fit the exposure scenario. MOEs were calculated based on each for both minimum and maximum label rates. MOEs were adequate when applicators were assumed to wear a single layer of clothing (long sleeved shirt and long pants) and mixers/loaders were assumed to wear chemical-resistant goves and a single layer of clothing. The Agency is requiring the registrant, through this RED, to develop appropriate exposure data in order to more accurately assess the risk associated with this use. This RED also requires mixers/loaders to wear chemical-resistant gloves and single layer body covering.

All applicators must wear single layer clothing in order to reduce potential exposure. Given the range of exposure values based on the databases used and the protective clothing that will be required to be worn when handling this pesticide, the Agency believes that workers will be adequately protected. Exposures and resultant risks will be assessed once the required data are available.

Post-Application

EPA has no concerns about post-application exposure at this time and no data are required at this time.

b. Environmental

(1) Avian

Acute

Diphenylamine is practically non-toxic to avian species on an acute and sub-acute basis. Since this is an indoor food use chemical, the Agency does not conduct avian risk assessments for indoor use chemicals. However, given the limited volume and pattern of diphenylamine use, the likelihood of adverse effects on ecological systems is considered to be minimal. There are no further data required.

Chronic

Diphenylamine does not represent a chronic risk to birds. Avian reproduction studies using the TGAI are not required for diphenylamine because of the indoor-food end-use.

(2) Mammals, Acute and Chronic

Diphenylamine does not represent an acute or chronic risk to mammals. Wild mammal testing is not required for diphenylamine because of the intended indoor-food end-use pattern.

(3) Insects

A honey bee acute contact study using the TGAI is not required for diphenylamine because its use will not result in honey bee exposure.

(4) Freshwater Fish

Diphenylamine represents a relatively low acute toxicity to fresh water fish. Hence, a freshwater fish early life-stage test using the TGAI is not required for diphenylamine because of the intended indoor-food end-use.

(5) Aquatic invertebrates

The acute toxicity to aquatic invertebrates is expected to be moderate. A freshwater chronic aquatic invertebrate life-cycle test using the TGAI is not required for diphenylamine because of the intended indoor-food end-use.

(6) Estuarine and Marine Organisms

Diphenylamine represents a relatively low toxicity to estuarine and marine organisms. Estuarine and marine testing is not required for diphenylamine because of the intended indoor-food end-use pattern.

(7) Nontarget Plants (Terrestrial, Semi-Aquatic, and Aquatic)

Diphenylamine represents a relatively low toxicity to non-target plants. Nontarget plant testing is not required for diphenylamine because of the intended indoor-food end-use pattern.

(8) Endangered Species

The use of diphenylamine is expected to have minimal adverse effect on ecological systems due to the unlikeliness of exposure..

(9) Surface Water

Since diphenylamine is used indoors only, it is highly unlikely that it will runoff to surface waters. However, if used outdoors there is a potential to reach surface waters via dissolved runoff events occurring immediately after application. The high rate of aqueous photolysis and the susceptibility of the chemical in aerobic environments indicate that if it were to reach surface waters, however, the chemical would be short lived. Discharge of effluent containing diphenylamine for manufacturing use is regulated by NPDES permit.

(10) Ground Water

Because of minimal expected adverse effect on ecological systems due to the unlikeliness of exposure, the usual statement concerning groundwater is not necessary for diphenylamine.

5. Restricted Use Classification

Restricted Use Classification is not applicable for current diphenylamine use.

6. Reference Dose Exceedance

Current diphenylamine usage does not exceed the reference dose limits established by available data and current tolerances.

7. Endangered Species Statement

The Agency has developed a program ("The Endangered Species Protection Program") to identify all pesticides whose use may cause adverse impacts on endangered and threatened species and to implement mitigation measures that will eliminate the adverse impacts. At present, the program is being implemented on an interim basis as described in a Federal Register notice (54 FR 27984-28008, July 3, 1989), and is providing information to pesticide users to help them protect these species on a voluntary basis. As currently planned, the final program will call for label modifications referring to required limitations on pesticide uses, typically as depicted in county-specific bulletins or by other site-specific mechanisms as specified by state partners. A final program, which may be altered from the interim program, will be described in a future Federal Register notice. The Agency is not imposing label modifications at this time through the RED. Rather, any requirements for product use modifications will occur in the future under the Endangered Species Protection Program.

8. Labeling Rationale

The 1992 Worker Protection Standard for Agricultural Pesticides (WPS) established certain worker-protection requirements (personal protective equipment, restricted entry intervals, etc.) to be specified on the label of all products that contain uses within the scope of the WPS. All currently registered uses of diphenylamine are within the scope of the the WPS.

At this time, all products containing diphenylamine are intended primarily for occupational use (i.e. mixed, loaded, and applied by commercial applicators only; generally not available to homeowners). No registered use is likely to involve applications at residential sites.

Requirements for Handlers

For each end-use product, personal protective equipment and engineering control requirements for pesticide handlers are set during reregistration as follows:

- Based on risks posed to handlers by the active ingredient, EPA may establish active-ingredient-specific (a-i specific) handler requirements for end-use products containing that active ingredient. If such risks are minimal, EPA may choose not to establish a-i-specific handler requirements.

- EPA establishes handler PPE requirements for most end-use products, based on each product's acute toxicity characteristics.

- If A-I-specific requirements have been established, they must be compared to the end-use-product-specific PPE. The more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product. Engineering controls are considered more stringent than PPE requirements.

Occupational-Use Products

EPA is establishing a-i-specific requirements for all occupational handlers for diphenylamine. EPA has no data upon which to assess the risk to handlers operating drenching equipment. In lieu of data, EPA roughly estimated potential exposure and risk using a range-finding technique. Surrogate mixer/loader data from PHED (ver. 1.1) was combined with flagger data in the assessment. These surrogate exposure scenarios are assumed to more closely duplicate the exposures to handlers involved in drive-thru drenching applicators than other exposure scenarios for which data are available. Due to EPA's lack of data to assess exposure to handlers participating in drenching operations, EPA is establishing requirements of single layer body protection for the drench operator. Persons involved in mixing, loading, and adjusting and maintaining the drench equipment must wear chemical-resistant gloves and single layer body protection. Persons who during the application remain inside the truck cab with the windows and doors closed need not wear the required personal protective equipment. If, however, drivers exit the truck cab in or immediately adjacent to the treatment area during the application, they must wear the required PPE.

Post-Application/Entry Restrictions

Occupational-Use Products

At this time, EPA has no concerns about post-application exposures to immediately following diphenylamine drenching of apples.

9. Spray Drift Advisory

The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation to develop the best spray drift management practices. The Agency is now requiring interim measures that must be placed on product labels/labeling as specified in Section V. Once the Agency completes its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, the Agency may impose further refinements in spray drift management practices to further reduce off-target drift and risks associated with this drift.

V. ACTIONS REQUIRED OF REGISTRANTS

This section specifies the data requirements and responses necessary for the reregistration of both manufacturing-use and end-use products.The DPA Task Force has agreed to submit to the Agency for approval all label amendments by January 1, 1998 on both the manufacturing-use product and end-use products.

A. Manufacturing-Use Products

1. Additional Generic Data Requirements

The generic data base supporting the reregistration of diphenylamine for the above eligible use has been reviewed and determined to be substantially complete. The following studies are required to be conducted on the generic active ingredient:

- **in vivo/in vitro** Rat Hepatocyte Unscheduled DNA Synthesis (UDS) Assay [Guideline 84-4]

- Subchronic Dog: to investigate methemoglobinemic effect [Guideline 82-1]

- Deposition Study

- UV/visible absorption [Guideline 830.7050]

- Registrant must either certify that the beginning materials and manufacturing process for the TGAI have not changed, or must submit an updated product chemistry package.

- An independent laboratory validation study is needed if the data collection method for meat and milk is to be used as an enforcement method.

The DPA Task Force has agreed to conduct the deposition study and any subsequent exposure studies required (based on the results of the deposition study) as conditions of registration. Submission of the deposition study and the dermal exposure study, if needed, will be included as a term and condition of all DPA registrations. Consequently, failure to submit these studies in a timely manner will result in automatic suspension of these registrations.

2. Labeling Requirements for Manufacturing-Use Products

The Agency is requiring that the diphenylamine manufacturing use labeling be revised to include only the indoor-food end-use (specifically restricted to post-harvest drenching treatment prior to storage). The "Environmental Hazards" section must include the following:

" This pesticide is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewage systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."

To remain in complaince with FIFRA, manufacturing use product (MP) labeling must be revised to comply with all current EPA regulations, PR Notices and applicable policies. The MP labeling must bear the following statement under Directions for Use:

"Only for formulation into a plant growth regulator used for reduction of scald on apples in storage."

An MP registrant may, at his/her discretion, add one of the following statements to an MP label under "Directions for Use" to permit the reformulation of the product for a specific use or all additional uses supported by a formulator or user group:

(a) "This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA data submission requirements regarding support of such use(s)."

(b) "This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s)."

All products distributed or sold by **registrants and distributors (supplemental registrants)** should bear labeling that is consistent with this notice by **January 1, 1998** and all products distributed or sold by **persons other than registrants or supplemental registrants** after **January 1, 1998** should bear correct labeling.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has

been made. Registrants must review previous data submissions to ensure that they meet current EPA acceptance criteria and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then study MRID numbers should be cited according to the instructions in the Requirement Status and Registrants Response Form provided for each product.

2. Labeling Requirements for End-Use Products

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. All end-use product labels [e.g. multiple active ingredient (MAI) labels, SLN's, and products subject to generic data exemption] must be amended such that they are consistent with the basic producer labels.

Diphenylamine labeling for end-use products must be revised to include only the indoor-food end-use (specifically restricted to post-harvest drenching treatment prior to storage). The "Environmental Hazards" section should include the following:

" This pesticide is toxic to fish and aquatic invertebrates. Do not contaminate water by cleaning of equipment or disposing of equipment washwater or rinsate."

Worker Protection Standard

Any product whose labeling reasonably permits use in the production of an agricultural plant 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 (4 0 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 with, and within the deadlines specified in, PR Notices 93-7 and 93-11. Unless otherwise specifically directed in this RED, 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 April 21, 1994, except as otherwise 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 the primary registrant or any supplementally registered distributor.

After October 23, 1995, except as otherwise 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.

PPE Requirements for Pesticide Handlers

For sole-active-ingredient end-use products that contain diphenylamine, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For multiple-active-ingredient end-use products that contain diphenylamine, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use

Active-Ingredient-Specific PPE or Engineering Control Requirements

EPA is establishing the following active-ingredient specific PPE for all handlers of diphenylamine end-use products.

"Handlers (including mixers, loaders, persons cleaning or maintaining the drencher equipment, and persons handling treated apples or apple containers still wet with drench) must wear:

--long-sleeved shirt and long pants
--chemical-resistant gloves*
Drenching applicators must wear:

--long-sleeved shirt and long pants

Exception: Persons who, during the application, remain inside the truck cab with the windows and doors closed need not wear the PPE required for other handlers. However, if such drivers exit the truck cab in or immediately adjacent to the treatment area during the application, then they must wear the required PPE."

* For the glove statement, use the statement established for diphenylamine through the instructions in Supplement Three of PR Notice 93-7.

PPE Requirements for End-use Product Labels

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active-ingredient specific

personal protective equipment specified above. The more protective PPE must be placed on the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7. The format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

PPE Requirements for End-Use Product Labels

The PPE, if any, that would be established on the basis of the acute toxicity category of each end-use product must be compared to the active-ingredient-specific personal protective equipment specified above. The more protective PPE must be placed on the product labeling. A requirement is considered more protective than a recommendation (e.g., "must wear" is more protective than "should wear"). For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7. The format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Entry Restrictions

For sole-active-ingredient end-use products that contain diphenylamine, the product labeling must be revised to adopt the entry restrictions set forth in this section. Any conflicting entry restrictions on the current labeling must be removed.

For multiple-active-ingredient end-use products that contain diphenylamine, the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Products Intended Primarily for Occupational Use

Entry restrictions:

The Agency is aware that all post-application handling of treated apples or apple containers are to be conducted by forklift machinery. However, if for any reason circumstanses arise whereby persons are manually handling treated apples or apple containers that are still wet with drench, then they must wear the same personal protective equipment as required for handlers. See section on handler PPE above for the required PPE.

Other Labeling Requirements

The Agency is requiring the following labeling statements to be located on all end-use products containing diphenylamine that are intended primarily for occupational use.

Application Restrictions

"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."

User Safety Requirements

“Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.”

“Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.”

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."
- "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Effluent Discharge Labeling Statements

Refer to subsection A. above for labeling requirements for effluent discharge.

C. Tolerance Revocation and Import Tolerances

No use of diphenylamine is being cancelled/voluntarily cancelled as part of EPA's reregistration eligibility decision regarding this pesticide. It is EPA's policy to propose revocation of a tolerance, and/or food/feed additive regulation, following the deletion of a related food use from a registration, or following the cancellation of a related food-use registration. As a result, any parties interested in supporting the tolerance/regulation for import purposes in the absence of a registered U.S. use should notify EPA as soon as possible.

In responding, EPA will provide detailed information on the outstanding data requirements for these tolerances and/or regulations. The Agency will consider commitments made to generate data to support such tolerances/regulations and the timeliness of data submissions in its assessment of whether the tolerances/regulations should be retained. Persons interested in establishing a new tolerance for import purposes only, or retaining a current tolerance for import purposes following cancellation of the related use, must submit a petition along with the appropriate fees and supporting data.

D. Existing Stocks

Registrants may generally distribute and sell products bearing old labels/labeling until December 31, 1997. Persons other than the registrant may generally distribute or sell such products for 50 months from the date of the issuance of this RED. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors. Refer to "Existing Stocks of Pesticide Products; Statement of Policy"; Federal Register, Volume 56, No. 123, June 26, 1991.

The Agency has determined that registrants may distribute and sell diphenylamine products bearing old labels/labeling for 26 months from the date of issuance of this RED. Persons other than the registrant may distribute or sell such products for 50 months from the date of the issuance of this RED. Registrants and persons other than registrants remain obligated to meet pre-existing Agency imposed label changes and existing stocks requirements applicable to products they sell or distribute.

VI. APPENDICES

Case 2210 [Diphenylamine] Chemical 038501 [Diphenylamine]

SITE Application Type, Application Timing, Application Equipment) Surface Type (Antimicrobial only) & Efficacy Influencing Factor (Antimicrobial only)	Form(s)	Min. Appl. Rate (AI unless noted otherwise)	Max. Appl. Rate (AI unless noted otherwise)	Soil Tex. Max. Dose	Max. # Apps @ Max. Rate /crop /year cycle	Max. Dose [(AI unless noted otherwise)/A] /crop /year cycle	Min. Interv (days)	Re-Entry Intv.	Geographic Limitations Allowed	Geographic Limitations Disallowed	Use Limitations Codes
USES ELIGIBLE FOR REREGISTRATION											
FOOD/FEED USES											
APPLE				Use Group: INDOOR FOOD							
Dip treatment, Postharvest, Dip tank	EC	NA	2.666 lb/159 gal	*	NS	NS	NS	NS	NS	NS	A26(2), A43(30), CAL, GD8
	WP	NA	1.66 lb/100 gal	*	NS	1/1 yr	NS	NS	NS	NS	A26(2), A43(30), C93, CAL, CCD(1), GI4
Drench, Postharvest, Drencher	EC	NA	2.666 lb/159 gal	*	NS	NS	NS	NS	NS	NS	A26(2), A43(30), CAL, GD8
	SC/L	NA	.002364 lb bu	*	NS	NS	NS	NS	NS	NS	C93, CAL, GD8
Flood treatment, Postharvest, Tank	WP	NA	1.66 lb/100 gal	*	NS	1/1 yr	NS	NS	NS	NS	A26(2), A43(30), C93, CAL, CCD(1),
		GI4									
Spray, Postharvest, Sprayer	EC	NA	2.666 lb/159 gal	*	NS	NS	NS	NS	NS	NS	A26(2), A43(30), CAL, GD8
	RTU	NA	UC	*	NS	NS	NS	NS	NS	NS	C04, CAL, GD8
	WP	NA	1.66 lb/100 gal	*	NS	1/1 yr	NS	NS	NS	NS	A26(2), A43(30), C93, CAL, CCD(1), GI4

APPENDIX A REPORT

Case 2210 [Diphenylamine] Chemical 038501 [Diphenylamine]
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LEGEND
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Sort: Uses Eligible or Ineligible for Re-registration, Food/Feed or Non-Food/Non-Feed Uses, Alpha Site Name, Use Group Name, Alpha Application Type/Timing/Equipment Description, Formulation, Maximum Application Rate Unit/Area Quantity, Minimum Application Rate

HEADER ABBREVIATIONS

Min. Appl. Rate (AI unless noted otherwise)	: Minimum dose for a single application to a single site. System calculated. Antimicrobial claims only.
Max. Appl. Rate (AI unless noted otherwise)	: Maximum dose for a single application to a single site. System calculated.
Soil Tex. Max. Dose	: Maximum dose for a single application to a single site as related to soil texture (Herbicide claims only).
Max. # Apps @ Max. Rate	: Maximum number of Applications at Maximum Dosage Rate. Example: "4 applications per year" is expressed as "4/1 yr"; "4 applications per 3 years" is expressed as "4/3 yr"
Max. Dose [(AI unless noted otherwise)/A]	: Maximum dose applied to a site over a single crop cycle or year. System calculated.
Min. Interv (days)	: Minimum Interval between Applications (days)
Re-Entry Intv.	: Reentry Intervals
PRD Report Date	: LUIS contains all products that were active or suspended (and that were available from OPP Document Center) as of this date. Some products registered after this date may have data included in this report, but LUIS does not guarantee that all products registered after this date have data that has been captured.

SOIL TEXTURE FOR MAX APP. RATE

*	: Non-specific
C	: Coarse
M	: Medium
F	: Fine
O	: Others

FORMULATION CODES

EC	: EMULSIFIABLE CONCENTRATE
RTU	: LIQUID-READY TO USE
SC/L	: SOLUBLE CONCENTRATE/LIQUID
WP	: WETTABLE POWDER

ABBREVIATIONS

AN	: As Needed
NA	: Not Applicable
NS	: Not Specified (on label)
UC	: Unconverted due to lack of data (on label), or with one of following units: bag, bait, bait block, bait pack, bait station, bait station(s), block, briquet, briquets, bursts, cake, can, canister, capsule, cartridges, coil, collar, container, dispenser, drop, eartag, grains, lure, pack, packet, packets, pad, part, parts, pellets, piece, pieces, pill, pumps, sec, sec burst, sheet, spike, stake, stick, strip, tab, tablet, tablets, tag, tape, towelette, tray, unit, --

APPLICATION RATE

DCNC	: Dosage Can Not be Calculated
No Calc	: No Calculation can be made
W	: PPM calculated by weight
V	: PPM Calculated by volume
U	: Unknown whether PPM is given by weight or by volume

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APPLICATION RATE (CONT.)
cwt : Hundred Weight
nnE-xx : nn times (10 power -xx); for instance, "1.234E-04" is equivalent to ".0001234"

USE LIMITATIONS CODES
A26 : __ minute(s) contact time (maximum).
A43 : __ seconds contact time (minimum).
C04 : Proper ventilation required.
C93 : Do not apply directly to water.
CAG : Do not apply where runoff is likely to occur.
CAL : Do not contaminate water, food or feed.
CCD : Do not make more than _____ applications per year.
GD8 : Do not use treated apples in the manufacture of livestock feeds.
GD9 : Do not graze cover crops.
GI4 : Do not use treated apples in the manufacture of pomace for use in livestock feeds.
* NUMBER IN PARENTHESES REPRESENTS THE NUMBER OF TIME UNITS (HOURS,DAYS, ETC.) DESCRIBED IN THE LIMITATION.

UNIT DESCRIPTIONS
bu : bushel
gal : gallon
lb : pound
tree : tree

GUIDE TO APPENDIX B

Appendix B contains listings of data requirements which support the reregistration for active ingredients within the case 2665 covered by this Reregistration Eligibility Decision Document. It contains generic data requirements that apply to 2665 in all products, including data requirements for which a "typical formulation" is the test substance.

The data table is organized in the following format:

1. Data Requirement (Column 1). The data requirements are listed in the order in which they appear in 40 CFR Part 158. the reference numbers accompanying each test refer to the test protocols set in the Pesticide Assessment Guidelines, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161 (703) 487-4650.

2. Use Pattern (Column 2). This column indicates the use patterns for which the data requirements apply. The following letter designations are used for the given use patterns:

A	Terrestrial food
B	Terrestrial feed
C	Terrestrial non-food
D	Aquatic food
E	Aquatic non-food outdoor
F	Aquatic non-food industrial
G	Aquatic non-food residential
H	Greenhouse food
I	Greenhouse non-food
J	Forestry
K	Residential
L	Indoor food
M	Indoor non-food
N	Indoor medical
O	Indoor residential

3. Bibliographic citation (Column 3). If the Agency has acceptable data in its files, this column lists the identifying number of each study. This normally is the Master Record Identification (MRID) number, but may be a "GS" number if no MRID number has been assigned. Refer to the Bibliography appendix for a complete citation of the study.

APPENDIX B

Data Supporting Guideline Requirements for the Reregistration of Diphenylamine

REQUIREMENT		USE PATTERN	CITATION(S)
PRODUCT CHEMISTRY			
61-1	Chemical Identity	all	43503901
61-2A	Start. Mat. & Mnfg. Process	all	43642001
61-2B	Formation of Impurities	all	43642001, 43503901
62-1	Preliminary Analysis	all	42795501, 43153301
62-3	Analytical Method	all	42795501, 43153301
63-2	Color	all	42716501
63-3	Physical State	all	42716501
63-4	Odor	all	42716501
63-5	Melting Point	all	42716501
63-7	Density	all	42716501
63-8	Solubility	all	42898801
63-9	Vapor Pressure	all	42876201
63-10	Dissociation Constant	all	42716401
63-11	Octanol/Water Partition	all	42826601
63-12	pH	all	42716501
63-13	Stability	all	42781501
ECOLOGICAL EFFECTS			
71-1A	Acute Avian Oral - Quail/Duck	all	43878901
71-2B	Avian Dietary - Duck	all	43879101
72-1C	Fish Toxicity Rainbow Trout	all	43879001
72-2A	Invertebrate Toxicity	all	43878301
TOXICOLOGY			
81-1	Acute Oral Toxicity - Rat	all	41899401

Data Supporting Guideline Requirements for the Reregistration of Diphenylamine

REQUIREMENT		USE PATTERN	CITATION(S)
81-2	Acute Dermal Toxicity - Rabbit/Rat	all	41899402
81-4	Primary Eye Irritation - Rabbit	all	41899404
81-5	Primary Dermal Irritation - Rabbit	all	41899405
81-6	Dermal Sensitization - Guinea Pig	all	43540801
82-1A	90-Day Feeding - Rodent	all	42339701
82-1B	90-Day Feeding - Non-rodent	all	00148521
82-2	21-Day Dermal - Rabbit/Rat	all	42304901
83-1A	Chronic Feeding Toxicity - Rodent	all	43401401, 43033601
83-1B	Chronic Feeding Toxicity - Non-Rodent	all	43000601
83-2A	Oncogenicity - Rat	all	43401401, 43033601
83-2B	Oncogenicity - Mouse	all	43369501, 43132401
83-3A	Developmental Toxicity - Rat	all	44165401
83-3B	Developmental Toxicity - Rabbit	all	00148521
83-4	2-Generation Reproduction - Rat	all	42638101
84-2A	Gene Mutation (Ames Test)	all	42312101, 42311901
84-2B	Structural Chromosomal Aberration	all	42311901, 42312001
84-4	Other Genotoxic Effects	all	42332101
85-1	General Metabolism	all	42994801
OCCUPATIONAL/RESIDENTIAL EXPOSURE			
231	Estimation of Dermal Exposure at Outdoor Sites	all	44212501
232	Estimation of Inhalation Exposure at Outdoor Sites	all	44212501
ENVIRONMENTAL FATE			
161-1	Hydrolysis	all	42660001
161-2	Photodegradation - Water	all	42958201

Data Supporting Guideline Requirements for the Reregistration of Diphenylamine

REQUIREMENT		USE PATTERN	CITATION(S)
162-1	Aerobic Soil Metabolism	all	42964201
162-3	Anaerobic Aquatic Metabolism	all	43080901
163-1	Leaching/Adsorption/ Desorption	all	43412701, 43413001
RESIDUE CHEMISTRY			
171-4A	Nature of Residue - Plants	all	43156201, 43370101, 42897301
171-4B	Nature of Residue - Livestock	all	43197101, 43187501
171-4C	Residue Analytical Method - Plants	all	43428401, 43428402, 43428403
171-4D	Residue Analytical Method - Animal	all	43973201
171-4E	Storage Stability	all	43620901
171-4J	Magnitude of Residues - Meat/Milk/Poultry/Egg	all	43972601
171-4K	Crop Field Trials	all	43625501
171-4L	Processed Food	all	43633601

GUIDE TO APPENDIX C

1. CONTENTS OF BIBLIOGRAPHY. This bibliography contains citations of all studies considered relevant by EPA in arriving at the positions and conclusions stated elsewhere in the Reregistration Eligibility Document. Primary sources for studies in this bibliography have been the body of data submitted to EPA and its predecessor agencies in support of past regulatory decisions. Selections from other sources including the published literature, in those instances where they have been considered, are included.

2. UNITS OF ENTRY. The unit of entry in this bibliography is called a "study". In the case of published materials, this corresponds closely to an article. In the case of unpublished materials submitted to the Agency, the Agency has sought to identify documents at a level parallel to the published article from within the typically larger volumes in which they were submitted. The resulting "studies" generally have a distinct title (or at least a single subject), can stand alone for purposes of review and can be described with a conventional bibliographic citation. The Agency has also attempted to unite basic documents and commentaries upon them, treating them as a single study.

3. IDENTIFICATION OF ENTRIES. The entries in this bibliography are sorted numerically by Master Record Identifier, or "MRID number". This number is unique to the citation, and should be used whenever a specific reference is required. It is not related to the six-digit "Accession Number" which has been used to identify volumes of submitted studies (see paragraph 4(d)(4) below for further explanation). In a few cases, entries added to the bibliography late in the review may be preceded by a nine character temporary identifier. These entries are listed after all MRID entries. This temporary identifying number is also to be used whenever specific reference is needed.

4. FORM OF ENTRY. In addition to the Master Record Identifier (MRID), each entry consists of a citation containing standard elements followed, in the case of material submitted to EPA, by a description of the earliest known submission. Bibliographic conventions used reflect the standard of the American National Standards Institute (ANSI), expanded to provide for certain special needs.

   a Author. Whenever the author could confidently be identified, the Agency has chosen to show a personal author. When no individual was identified, the Agency has shown an identifiable laboratory or testing facility as the author. When no author or laboratory could be identified, the Agency has shown the first submitter as the author.

   b. Document date. The date of the study is taken directly from the document. When the date is followed by a question mark, the bibliographer has deduced the date from the evidence contained in the document. When the date appears

as (19??), the Agency was unable to determine or estimate the date of the document.

c. Title. In some cases, it has been necessary for the Agency bibliographers to create or enhance a document title. Any such editorial insertions are contained between square brackets.

d. Trailing parentheses. For studies submitted to the Agency in the past, the trailing parentheses include (in addition to any self-explanatory text) the following elements describing the earliest known submission:

(1) Submission date. The date of the earliest known submission appears immediately following the word "received."

(2) Administrative number. The next element immediately following the word "under" is the registration number, experimental use permit number, petition number, or other administrative number associated with the earliest known submission.

(3) Submitter. The third element is the submitter. When authorship is defaulted to the submitter, this element is omitted.

(4) Volume Identification (Accession Numbers). The final element in the trailing parentheses identifies the EPA accession number of the volume in which the original submission of the study appears. The six-digit accession number follows the symbol "CDL," which stands for "Company Data Library." This accession number is in turn followed by an alphabetic suffix which shows the relative position of the study within the volume.

BIBLIOGRAPHY

MRID	CITATION

00148521 Edwards, J.; Leeming, N.; Clark, R.; et al. (1983) Effect of Diphenylamine on Pregnancy of the New Zealand White Rabbit: HRC Report No. PWT 1/2/83409. Unpublished study prepared by Huntingdon Research Centre. 80 p.

00148523 Spanjers, M.; Til, H. (1982) Determination of the Acute Oral Toxicity of Diphenylamine in Rats: Report No. V 82.263/220060. Unpublished study prepared by Netherlands Organization for Applied Scientific Research. 14 p.

00148524 Van Beek, L.; Bruijntjes, J. (1982) Acute Dermal Toxicity Study with Diphenylamine in Albino Rabbits: B82/993. Unpublished study prepared by Institute CIVO-Toxicology and Nutrition TNO. 4 p.

00148525 Van Beek, L. (1982) Eye Irritation Test with Diphenylamine in Albino Rabbits: B 82-61-23. Unpublished study prepared by CIVO-Toxicology and Nutrition TNO. 7 p.

00148533 Decco Tiltbelt (1984) Current Practices and Residues: ?Diphenylamine in or on Applesσ. Unpublished compilation. 30 p.

41899401 Majnarich, J. (1991) Diphenylamine-Super Refined-Acute Oral to Toxicity, LD 50 (Rat): Lab Project Number: 022-91. Unpublished Study prepared by Bioconsultants, Inc. 13 p.

41899402 Majnarich, J. (1991) Diphenylamine-Super Refined-Dermal LD 50. : Lab Project Number: 024-91. Unpublished study prepared by Bioconsultants, Inc. 20 p.

41899403 Majnarich, J. (1991) Diphenylamine-Super Refined-Dermal Sensitization Study: Lab Project Number: 023-91. Unpublished study prepared by Bioconsultants, Inc. 13 p.

41899404 Kreuzmann, J. (1991) Primary Eye Irritation Study in Rabbits Without Rinsing With Diphenylamine Super-Refined: Lab Project Number 91-8052-21 (B). Unpublished study prepared by Hill Top Biolabs, Inc. 32 p.

41899405 Kreuzmann, J. (1991) Primary Skin Irritation Study in Rabbits With Diphenylamine Super-Refined: Lab Project Number: 91-8052-21 (A). Unpublished study prepared by Hill Top Biolabs, Inc. 30 p.

42292001 Rodwell, D. (1992) Teratology Study in Rats with Diphenylamine (DPA): Final Report: Lab Project Number: 3255.3. Unpublished study prepared by Springborn Laboratories, Inc. 267 p.

BIBLIOGRAPHY

MRID **CITATION**

42304901 Siglin, J. (1992) 21-Day Dermal Toxicity Study in Rabbits with Diphenylamine (DPA): Final Report: Lab Project Number: 3255. 1. Unpublished study prepared by Springborn Labs, Inc. 257 p.

42312001 Murli, H. (1992) Mutagenicity Test on Diphenylamine in vivo Mammalian Micronucleus Assay: Lab Project Number: 14902-0-455. Unpublished study prepared by Hazleton Washington, Inc. 52 p.

42312101 Lawlor, T. (1992) Mutagenicity Test on Diphenylamine in the Salmonella/Mammalian-Microsome Reverse Mutation Assay (Ames Test): Lab Project Number: 14902-0-401. Unpublished study prepared by Hazleton Washington, Inc. 67 p.

42332101 Cifone, M. (1992) Mutagenicity Test on Diphenylamine in the L5178Y TK + /Mouse Lymphoma Forward Mutation Assay: Lab Project Number: 14902-0-431. Unpublished study prepared by Hazleton Washington, Inc. 74 p.

42339701 Krohmer, R. (1992) 90-Day Subchronic Toxicity Evaluation of Diphenylamine in Rats: Lab Project Number: 426C-101-034-91. Unpublished study prepared by T.P.S., Inc. 382 p.

42339801 Krohmer, R. (1992) 90 Day Evaluation of Diphenylamine in the Dog: Lab Project Number: 426A-501-034-91. Unpublished study prepared by T.P.S., Inc. 308 p.

42542801 Botta, J. (1992) 90 Day Subchronic Toxicity Evaluation of Diphenylamine in the Mouse: Lab Project Number: 426E-001-034-91. Unpublished study prepared by TPS, Inc. 449 p.

42638101 Rodwell, D. (1993) Two Generation Reproduction Study in Rats with Diphenylamine (DPA): Final Report: Lab Project Number: 3255.4. Unpublished study prepared by Springborn Laboratories, Inc. 1185 p.

42660001 Baur, L. (1993) Hydrolysis of (carbon 14)-Ring-Diphenylamine in Water at pH 5, 7, and 9: Lab Project Number: XBL 92084: RPT00119. Unpublished study prepared by XenoBiotic Labs, Inc. 82 p.

42897301 Kim-Kang, H. (1993) Metabolism of (carbon 14)-Diphenylamine in Stores Apples--Nature of the Residue in Plants: Final Report: Lab No: XBL/91071: RPT00124. Unpublished study prepared by XenoBiotic Laboratories, Inc. 300 p.

BIBLIOGRAPHY

MRID	CITATION

42958201 Baur, L.; Robinson, R. (1993) Aqueous Photolysis of (carbon 14)-Ring-Diphenylamine: Lab Project Number: XBL 92087: RPT00123. Unpublished study prepared by XenoBiotic Laboratories, Inc. 106 p.

42964201 Liu, D. (1993) Aerobic Soil Metabolism of (carbon 14)-Ring-Diphenylamine: Lab Project Number: XBL 92082: RPT00139. Unpublished study prepared by XenoBiotic Labs, Inc. 98 p.

42994801 Wu, D. (1993) Diphenylamine: Rat Metabolism Study: Final Report: Lab Project Number: 92081: RPT00131. Unpublished study prepared by XenoBiotic Laboratories, Inc. 342 p.

43000601 Botta, J. (1993) One Year Chronic Study of Diphenylamine in Dogs: Lab Project Number: 426B-502-044-91. Unpublished study prepared by T.P.S., Inc. 624 p.

43080901 Liu, D. (1993) Anaerobic Aquatic Metabolism of (carbon 14)-Ring-Diphenylamine: Lab Project Number: 92083: RPT00140. Unpublished study prepared by XenoBiotic Labs, Inc. 102 p.

43156201 Kim-Kang, H. (1994) Metabolism of (carbon 14)-Diphenylamine in Stored Apples--Nature of the Residue in Plants: Addendum: Lab Project Number: XBL 91071: RPT00124. Unpublished study prepared by XenoBiotic Labs, Inc. 54 p.

43163501 Tshabalala, M. (1994) Determination of Diphenylamine Residues in Apples and Processed Apple Fractions by Gas Chromatography (GC) with Mass-Selective Detection (MSD): Final Report: Lab Project Number: HWI 6524-100: MP-DPAP-MA. Unpublished study prepared by Hazleton Wisconsin, Inc. 37 p.

43187501 Kim-Kang, H. (1994) Metabolism of (carbon 14)Diphenylamine in the Laying Hen: Lab Project Number: XBL 93041: RPT00161. Unpublished study prepared by XenoBiotic Labs., Inc. 264 p.

43197101 Kim-Kang, H. (1994) Metabolism of (carbon 14)Diphenylamine in Lactating Goats: Lab Project Number: XBL 92089: RPT00150: WIL-207001. Unpublished study prepared by XenoBiotic Labs., Inc. and WIL Research Labs., Inc. 416 p.

43369501 Botta, J. (1994) 18 Month Oncogenicity Evaluation of Diphenylamine in the Mouse: Lab Project Number: 426H/002/646/91. Unpublished study prepared by T.P.S., Inc. 2348 p.

BIBLIOGRAPHY

MRID	CITATION
43370101	Kim-Kang, H. (1994) Metabolism of (carbon 14)-Diphenylamine in Stored Apples--Nature of the Residue in Plants: Addendum (to Original and Addendum Reports): Lab Project Number: XBL 91071: RPT00124. Unpublished study prepared by XenoBiotic Labs, Inc. 45 p.
43401401	Botta, J. (1994) 24 Month Combined Oncogenicity/Toxicity Evaluation of Diphenylamine in Rats: Final Report: Lab Project Number: 426D-102-048-91. Unpublished study prepared by T.P.S., Inc. 3421 p.
43412701	Reynolds, J. (1994) Adsorption and Desorption of (carbon 14)-Ring-Diphenylamine in Four Soils and One Sediment: Lab Project Number: 92086: RPT00163. Unpublished study prepared by XenoBiotic Lab., Inc. 123 p.
43413001	Kammerer, R. (1994) Aged Leaching of ((carbon 14)-Ring) Diphenylamine in Four Soils: Lab Project Number: XBL94011: RPT00184. Unpublished study prepared by XenoBiotic Lab., Inc. 139 p.
43428401	Tshabalala, M. (1994) Amendment No. 1 to the Report Determination of Diphenylamine Residues in Apples and Processed Apple Fractions by Gas Chromatography (GC) with Mass-Selective Detection (MSD): Lab Project Number: HWI 6524-100. Unpublished study prepared by Hazleton Wisconsin, Inc. 5 p.
43428402	Tshabalala, M. (1994) Amendment No. 2 to the Report Determination of Diphenylamine Residues in Apples and Processed Apple Fractions by Gas Chromatography (GC) with Mass-Selective Detection (MSD): Lab Project Number: HWI 6524-100. Unpublished study prepared by Hazleton Wisconsin, Inc. 5 p.
43428403	Clark, A. (1994) Validation of a Method for the Determination of Diphenylamine Residues in Apples and Processed Apple Fractions by Gas Chromatography (GC) with Mass-Selective Detection (MSD): Lab Project Number: 3716-F. Unpublished study prepared by Midwest Research Institute. 67 p.
43540801	Kiplinger, G. (1995) Skin Sensitization Study of Diphenylamine Technical in Albino Guinea Pigs: Final Report: Lab Project Number: WIL-256001. Unpublished study prepared by WIL Research Labs, Inc. 49 p.
43620901	Johnson, G.; Strickland, M.(1995) Storage Stability of Residues of Diphenylamine in/on Fresh Apples, Apple Juice, and Wet and Dried Pomace: Lab Project Number: Final Report: 101/003: DPA/ 93/03. Unpublished study prepared by Western EcoSystems Technology and Hazleton Wisconsin. 302 p.

BIBLIOGRAPHY

MRID	CITATION

43625501 Johnson, G.; Strickland, M. (1995) Magnitude of Residues in/on Fresh and Stored Apples After Post-harvest Treatment with Diphenylamine: Final Report: Lab Project Number: DPA 93-01. Unpublished study prepared by Western Ecosystems Technology (WEST, Inc.). 272 p.

43633601 Johnson, G.; Strickland, M. (1995) Magnitude of Residues in/on Apple Juice and Wet and Dried Pomace Processed from Fruit Treated Post-Harvest with Diphenylamine: Final Report: Lab Project Number: DPA 93-02: MP-DPAP-MA: HWI 6524-103. Unpublished study prepared by Western Ecosystems Technology (WEST, Inc.); Wm. J. Englar & Assoc.; and Hazleton Wisconsin. 406 p.

43878301 Drottar, K.; Swigert, J. (1995) Diphenylamine Technical: A 48-Hour Flow-Through Acute Toxicity Test with the Cladoceran (Daphnia magna): Final Report: Lab Project Number: SDR20: 436A-102: MP-DPAP-MA. Unpublished study prepared by Wildlife International Ltd. 97 p.

43879001 Drottar, K.; Swigert, J. (1995) Diphenylamine Technical: A 96-Hour Flow-Through Acute Toxicity Test with the Rainbow Trout (Oncorhynchus mykiss): Final Report: Lab Project Number: SDR20: 436A-101: 436/100295/RBT-96H2/CHP105. Unpublished study prepared by Wildlife International Ltd. 99 p.

43879101 Palmer, S.; Beavers, J. (1995) Diphenylamine: A Dietary LC50 Study with the Mallard: Lab Project Number: DLR52: 436-101: 436/100295/MLCSDT.WC/ CHP105. Unpublished study prepared by Wildlife International Ltd. 74 p.

43972601 Keller, G.; Weber, K. (1996) Magnitude of the Residues of Diphenylamine in Edible Tissues and Milk of Lactating Dairy Cows: Final Report: Lab Project Number: CHW 6524-110. Unpublished study prepared by Corning Hazleton, Inc. 347 p.

43973201 Keller, G.; Weber, K. (1996) Validation of the Method for the Determination of Diphenylamine Using Milk and Tissues From a Lactating Goat Metabolism Study: Final Report: Lab Project Number: CHW 6524-112: CHW 6524-110. Unpublished study prepared by Corning Hazleton Inc. 93 p.

44212501 Wise, J. (1997) Estimation of Dermal and Inhalation Exposure at Apple Drenching Sites for Diphenylamine: Lab Project Number: S&A-970101: 97DPA0001: 970101. Unpublished study prepared by Seiler & Associates Inc. 46 p.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

GENERIC AND PRODUCT SPECIFIC DATA CALL-IN NOTICE

CERTIFIED MAIL

Dear Sir or Madam:

This Notice requires you and other registrants of pesticide products containing the active ingredient identified in Attachment A of this Notice, the Data Call-In Chemical Status Sheet, to submit certain data as noted herein to the U.S. Environmental Protection Agency (EPA, the Agency). These data are necessary to maintain the continued registration of your product(s) containing this active ingredient. Within 90 days after you receive this Notice you must respond as set forth in Section III below. Your response must state:

1. How you will comply with the requirements set forth in this Notice and its Attachments 1 through 7; or

2. Why you believe you are exempt from the requirements listed in this Notice and in Attachment 3 (for both generic and product specific data), the Requirements Status and Reqistrant's Response Form, (see section III-B); or

3. Why you believe EPA should not require your submission of data in the manner specified by this Notice (see section III-D).

If you do not respond to this Notice, or if you do not satisfy EPA that you will comply with its requirements or should be exempt or excused from doing so, then the registration of your product(s) subject to this Notice will be subject to suspension. We have provided a list of all of your products subject to this Notice in Attachment 2. All products are listed on both the generic and product specific Data Call-In Response Forms. Also included is a list of all registrants who were sent this Notice (Attachment 5).

The authority for this Notice is section 3(c)(2)(B) of the Federal Insecticide, Fungicide and Rodenticide Act as amended (FIFRA), 7 U.S.C. section 136a(c)(2)(B). Collection of this

information is authorized under the Paperwork Reduction Act by OMB Approval No. 2070-0107 and 2070-0057 (expiration date 3-31-99).

This Notice is divided into six sections and seven Attachments. The Notice itself contains information and instructions applicable to all Data Call-In Notices. The Attachments contain specific chemical information and instructions. The six sections of the Notice are:

Section I - Why You are Receiving this Notice
Section II - Data Required by this Notice
Section III - Compliance with Requirements of this Notice
Section IV - Consequences of Failure to Comply with this Notice
Section V - Registrants' Obligation to Report Possible Unreasonable Adverse Effects
Section VI - Inquiries and Responses to this Notice

The Attachments to this Notice are:

1 - Data Call-In Chemical Status Sheet
2 - Generic Data Call-In and Product Specific Data Call-In Response Forms with Instructions (Form A)
3 - Generic Data Call-In and Product Specific Data Call-In Requirements Status and Registrant's Response Forms with Instructions (Form B)
4 - EPA Batching of End-Use Products for Meeting Acute Toxicology Data Requirements for Reregistration
5 - List of Registrants Receiving This Notice
6 - Cost Share and Data Compensation Forms

SECTION I. WHY YOU ARE RECEIVING THIS NOTICE

The Agency has reviewed existing data for this active ingredient(s) and reevaluated the data needed to support continued registration of the subject active ingredient(s). This reevaluation identified additional data necessary to assess the health and safety of the continued use of products containing this active ingredient(s). You have been sent this Notice because you have product(s) containing the subject active ingredients.

SECTION II. DATA REQUIRED BY THIS NOTICE

II-A. DATA REQUIRED

The data required by this Notice are specified in the Requirements Status and Registrant's Response Forms: Attachment 3 (for both generic and product specific data requirements). Depending on the results of the studies required in this Notice, additional studies/testing may be required.

II-B. SCHEDULE FOR SUBMISSION OF DATA

You are required to submit the data or otherwise satisfy the data requirements specified in the Requirements Status and Registrant's Response Forms (Attachment 3) within the timeframes provided.

II-C. TESTING PROTOCOL

All studies required under this Notice must be conducted in accordance with test standards outlined in the Pesticide Assessment Guidelines for those studies for which guidelines have been established.

These EPA Guidelines are available from the National Technical Information Service (NTIS), Attn: Order Desk, 5285 Port Royal Road, Springfield, Va 22161 (Telephone number: 703-487-4650).

Protocols approved by the Organization for Economic Cooperation and Development (OECD) are also acceptable if the OECD recommended test standards conform to those specified in the Pesticide Data Requirements regulation (40 CFR § 158.70). When using the OECD protocols, they should be modified as appropriate so that the data generated by the study will satisfy the requirements of 40 CFR § 158. Normally, the Agency will not extend deadlines for complying with data requirements when the studies were not conducted in accordance with acceptable standards. The OECD protocols are available from OECD, 2001 L Street, N.W., Washington, D.C. 20036 (Telephone number 202-785-6323; Fax telephone number 202-785-0350).

All new studies and proposed protocols submitted in response to this Data Call-In Notice must be in accordance with Good Laboratory Practices [40 CFR Part 160].

II-D. REGISTRANTS RECEIVING PREVIOUS SECTION 3(c)(2)(B) NOTICES ISSUED BY THE AGENCY

Unless otherwise noted herein, this Data Call-In does not in any way supersede or change the requirements of any previous Data Call-In(s), or any other agreements entered into with the Agency pertaining to such prior Notice. Registrants must comply with the requirements of all Notices to avoid issuance of a Notice of Intent to Suspend their affected products.

SECTION III. COMPLIANCE WITH REQUIREMENTS OF THIS NOTICE

You must use the correct forms and instructions when completing your response to this Notice. The type of Data Call-In you must comply with (Generic or Product Specific) is specified in item number 3 on the four Data Call-In forms (Attachments 2 and 3).

III-A. SCHEDULE FOR RESPONDING TO THE AGENCY

The appropriate responses initially required by this Notice for generic and product specific data must be submitted to the Agency within 90 days after your receipt of this Notice.

Failure to adequately respond to this Notice within 90 days of your receipt will be a basis for issuing a Notice of Intent to Suspend (NOIS) affecting your products. This and other bases for issuance of NOIS due to failure to comply with this Notice are presented in Section IV-A and IV-B.

III-B. OPTIONS FOR RESPONDING TO THE AGENCY

1. Generic Data Requirements

The options for responding to this Notice for generic data requirements are: (a) voluntary cancellation, (b) delete use(s), (c) claim generic data exemption, (d) agree to satisfy the generic data requirements imposed by this Notice or (e) request a data waiver(s).

A discussion of how to respond if you choose the Voluntary Cancellation option, the Delete Use(s) option or the Generic Data Exemption option is presented below. A discussion of the various options available for satisfying the generic data requirements of this Notice is contained in Section III-C. A discussion of options relating to requests for data waivers is contained in Section III-D.

Two forms apply to generic data requirements, one or both of which must be used in responding to the Agency, depending upon your response. These two forms are the Data-Call-In Response Form, and the Requirements Status and Registrant's Response Form, (contained in Attachments 2 and 3, respectively).

The Data Call-In Response Forms must be submitted as part of every response to this Notice. The Requirements Status and Registrant's Response Forms also must be submitted if you do not qualify for a Generic Data Exemption or are not requesting voluntary cancellation of your registration(s). Please note that the company's authorized representative is required to sign the first page of both Data Call-In Response Forms and the Requirements Status and Registrant's Response Forms (if this form is required) and initial any subsequent pages. The forms contain separate detailed instructions on the response options. Do not alter the printed material. If you have questions or need assistance in preparing your response, call or write the contact person(s) identified in Attachment 1.

a. Voluntary Cancellation -

You may avoid the requirements of this Notice by requesting voluntary cancellation of your product(s) containing the active ingredient that is the subject of this Notice. If you wish to voluntarily cancel your product, you must submit completed Generic and Product Specific Data Call-In Response Forms (Attachment 2), indicating your election of this option. Voluntary cancellation is item number 5 on both Data Call-In Response Form(s). If you choose this option, these are the only forms that you are required to complete.

If you chose to voluntarily cancel your product, further sale and distribution of your product after the effective date of cancellation must be in accordance with the Existing Stocks provisions of this Notice, which are contained in Section IV-C.

b. Use Deletion -

You may avoid the requirements of this Notice by eliminating the uses of your product to which the requirements apply. If you wish to amend your registration to delete uses, you must submit the Requirements Status and Reqistrant's Response Form (Attachment 3), a completed application for amendment, a copy of your proposed amended labeling, and all other information required for processing the application. Use deletion is option number 7 under item 9 in the instructions for the Requirements Status and Reqistrant's Response Forms. You must also complete a Data Call-In Response Form by signing the certification, item number 8. Application forms for amending registrations may be obtained from the Registration Support Branch, Registration Division, Office of Pesticide Programs, EPA, by calling (703) 308-8358.

If you choose to delete the use(s) subject to this Notice or uses subject to specific data requirements, further sale, distribution, or use of your product after one year from the due date of your 90 day response, is allowed only if the product bears an amended label.

c. Generic Data Exemption -

Under section 3(c)(2)(D) of FIFRA, an applicant for registration of a product is exempt from the requirement to submit or cite generic data concerning an active ingredient if the active ingredient in the product is derived exclusively from purchased, registered pesticide products containing the active ingredient. EPA has concluded, as an exercise of its discretion, that it normally will not suspend the registration of a product which would qualify and continue to qualify for the generic data exemption in section 3(c)(2)(D) of FIFRA. To qualify, all of the following requirements must be met:

(i). The active ingredient in your registered product must be present solely because of incorporation of another registered product which contains the subject active ingredient and is purchased from a source not connected with you;

(ii). Every registrant who is the ultimate source of the active ingredient in your product subject to this DCI must be in compliance with the requirements of this Notice and must remain in compliance; and

(iii). You must have provided to EPA an accurate and current "Confidential Statement of Formula" for each of your products to which this Notice applies.

To apply for the Generic Data Exemption you must submit a completed Data Call-In Response Form, Attachment 2 and all supporting documentation. The Generic Data Exemption is item number 6a on the Data Call-In Response Form. If you claim a generic data exemption you are not required to complete the Requirements Status and Registrant's Response Form. Generic Data Exemption cannot be selected as an option for responding to product specific data requirements.

If you are granted a Generic Data Exemption, you rely on the efforts of other persons to provide the Agency with the required data. If the registrant(s) who have committed to generate and submit the required data fail to take appropriate steps to meet requirements or are no longer in compliance with this Data Call-In Notice, the Agency will consider that both they and you are not compliance and will normally initiate proceedings to suspend the registrations of both your and their product(s), unless you commit to submit and do submit the required data within the specified time. In such cases the Agency generally will not grant a time extension for submitting the data.

d. Satisfying the Generic Data Requirements of this Notice

There are various options available to satisfy the generic data requirements of this Notice. These options are discussed in Section III-C.1. of this Notice and comprise options 1 through 6 of item 9 in the instructions for the Requirements Status and Registrant's Response Form and item 6b on the Data Call-In Response Form. If you choose item 6b (agree to satisfy the generic data requirements), you must submit the Data Call-In Response Form and the Requirements Status and Registrant's Response Form as well as any other information/data pertaining to the option chosen to address the data requirement. Your response must be on the forms marked "GENERIC" in item number 3.

e. Request for Generic Data Waivers.

Waivers for generic data are discussed in Section III-D.1. of this Notice and are covered by options 8 and 9 of item 9 in the instructions for the Requirements Status and Registrant's Response Form. If you choose one of these options, you must submit both forms as well as any other information/data pertaining to the option chosen to address the data requirement.

2. Product Specific Data Requirements

The options for responding to this Notice for product specific data are: (a) voluntary cancellation, (b) agree to satisfy the product specific data requirements imposed by this Notice or (c) request a data waiver(s).

A discussion of how to respond if you choose the Voluntary Cancellation option is presented below. A discussion of the various options available for satisfying the product specific data requirements of this Notice is contained in Section III-C.2. A discussion of options relating to requests for data waivers is contained in Section III-D.2.

Two forms apply to the product specific data requirements one or both of which must be used in responding to the Agency, depending upon your response. These forms are the Data-Call-In Response Form, and the Requirements Status and Registrant's Response Form, for product specific data (contained in Attachments 2 and 3, respectively). The Data Call-In Response Form must be submitted as part of every response to this Notice. In addition, one copy of the Requirements Status and Registrant's Response Form also must be submitted for each product listed on the Data Call-In Response Form unless the voluntary cancellation option

is selected. Please note that the company's authorized representative is required to sign the first page of the Data Call-In Response Form and Requirements Status and Reqistrant's Response Form (if this form is required) and initial any subsequent pages. The forms contain separate detailed instructions on the response options. Do not alter the printed material. If you have questions or need assistance in preparing your response, call or write the contact person(s) identified in Attachment 1.

a. Voluntary Cancellation

You may avoid the requirements of this Notice by requesting voluntary cancellation of your product(s) containing the active ingredient that is the subject of this Notice. If you wish to voluntarily cancel your product, you must submit a completed Data Call-In Response Form, indicating your election of this option. Voluntary cancellation is item number 5 on both the Generic and Product Specific Data Call-In Response Forms. If you choose this option, you must complete both Data Call-In response forms. These are the only forms that you are required to complete.

If you choose to voluntarily cancel your product, further sale and distribution of your product after the effective date of cancellation must be in accordance with the Existing Stocks provisions of this Notice which are contained in Section IV-C.

b. Satisfying the Product Specific Data Requirements of this Notice.

There are various options available to satisfy the product specific data requirements of this Notice. These options are discussed in Section III-C.2. of this Notice and comprise options 1 through 6 of item 9 in the instructions for the product specific Requirements Status and Reqistrant's Response Form and item numbers 7a and 7b (agree to satisfy the product specific data requirements for an MUP or EUP as applicable) on the product specific Data Call-In Response Form. Note that the options available for addressing product specific data requirements differ slightly from those options for fulfilling generic data requirements. Deletion of a use(s) and the low volume/minor use option are not valid options for fulfilling product specific data requirements. It is important to ensure that you are using the correct forms and instructions when completing your response to the Reregistration Eligibility Decision document.

c. Request for Product Specific Data Waivers.

Waivers for product specific data are discussed in Section III-D.2. of this Notice and are covered by option 7 of item 9 in the instructions for the Requirements Status and Registrant's Response Form. If you choose this option, you must submit the Data Call-In Response Form and the Requirements Status and Registrant's Response Form as well as any other information/data pertaining to the option chosen to address the data requirement. Your response must be on the forms marked "PRODUCT SPECIFIC" in item number 3.

III-C SATISFYING THE DATA REQUIREMENTS OF THIS NOTICE

1. Generic Data

If you acknowledge on the Generic Data Call-In Response Form that you agree to satisfy the generic data requirements (i.e. you select item number 6b), then you must select one of the six options on the Generic Requirements Status and Registrant's Response Form related to data production for each data requirement. Your option selection should be entered under item number 9, "Registrant Response." The six options related to data production are the first six options discussed under item 9 in the instructions for completing the Requirements Status and Registrant's Response Form. These six options are listed immediately below with information in parentheses to guide you to additional instructions provided in this Section. The options are:

(1) I will generate and submit data within the specified timeframe (Developing Data)
(2) I have entered into an agreement with one or more registrants to develop data jointly (Cost Sharing)
(3) I have made offers to cost-share (Offers to Cost Share)
(4) I am submitting an existing study that has not been submitted previously to the Agency by anyone (Submitting an Existing Study)
(5) I am submitting or citing data to upgrade a study classified by EPA as partially acceptable and upgradeable (Upgrading a Study)
(6) I am citing an existing study that EPA has classified as acceptable or an existing study that has been submitted but not reviewed by the Agency (Citing an Existing Study)

Option 1. Developing Data

If you choose to develop the required data it must be in conformance with Agency deadlines and with other Agency requirements as referenced herein and in the attachments. All data generated and submitted must comply with the Good Laboratory Practice (GLP) rule (40 CFR Part 160), be conducted according to the Pesticide Assessment Guidelines (PAG) and be in conformance with the requirements of PR Notice 86-5. In addition, certain studies require Agency approval of test protocols in advance of study initiation. Those studies for which a protocol must be submitted have been identified in the Requirements Status and Registrant's Response Form and/or footnotes to the form. If you wish to use a protocol which differs from the options discussed in Section II-C of this Notice, you must submit a detailed description of the proposed protocol and your reason for wishing to use it. The Agency may choose to reject a protocol not specified in Section II-C. If the Agency rejects your protocol you will be notified in writing, however, you should be aware that rejection of a proposed protocol will not be a basis for extending the deadline for submission of data.

A progress report must be submitted for each study within 90 days from the date you are required to commit to generate or undertake some other means to address that study requirement, such as making an offer to cost share or agreeing to share in the cost of developing that study. This 90-day progress report must include the date the study was or will

be initiated and, for studies to be started within 12 months of commitment, the name and address of the laboratory(ies) or individuals who are or will be conducting the study.

In addition, if the time frame for submission of a final report is more than 1 year, interim reports must be submitted at 12 month intervals from the date you are required to commit to generate or otherwise address the requirement for the study. In addition to the other information specified in the preceding paragraph, at a minimum, a brief description of current activity on and the status of the study must be included as well as a full description of any problems encountered since the last progress report.

The time frames in the Requirements Status and Registrant's Response Form are the time frames that the Agency is allowing for the submission of completed study reports or protocols. The noted deadlines run from the date of the receipt of this Notice by the registrant. If the data are not submitted by the deadline, each registrant is subject to receipt of a Notice of Intent to Suspend the affected registration(s).

If you cannot submit the data/reports to the Agency in the time required by this Notice and intend to seek additional time to meet the requirements(s), you must submit a request to the Agency which includes: (1) a detailed description of the expected difficulty and (2) a proposed schedule including alternative dates for meeting such requirements on a step-by-step basis. You must explain any technical or laboratory difficulties and provide documentation from the laboratory performing the testing. While EPA is considering your request, the original deadline remains. The Agency will respond to your request in writing. If EPA does not grant your request, the original deadline remains. Normally, extensions can be requested only in cases of extraordinary testing problems beyond the expectation or control of the registrant. Extensions will not be given in submitting the 90-day responses. Extensions will not be considered if the request for extension is not made in a timely fashion; in no event shall an extension request be considered if it is submitted at or after the lapse of the subject deadline.

Option 2. Agreement to Share in Cost to Develop Data

If you choose to enter into an agreement to share in the cost of producing the required data but will not be submitting the data yourself, you must provide the name of the registrant who will be submitting the data. You must also provide EPA with documentary evidence that an agreement has been formed. Such evidence may be your letter offering to join in an agreement and the other registrant's acceptance of your offer, or a written statement by the parties that an agreement exists. The agreement to produce the data need not specify all of the terms of the final arrangement between the parties or the mechanism to resolve the terms. Section 3(c)(2)(B) provides that if the parties cannot resolve the terms of the agreement they may resolve their differences through binding arbitration.

Option 3. Offer to Share in the Cost of Data Development

If you have made an offer to pay in an attempt to enter into an agreement or amend an existing agreement to meet the requirements of this Notice and have been unsuccessful, you

may request EPA (by selecting this option) to exercise its discretion not to suspend your registration(s), although you do not comply with the data submission requirements of this Notice. EPA has determined that as a general policy, absent other relevant considerations, it will not suspend the registration of a product of a registrant who has in good faith sought and continues to seek to enter into a joint data development/cost sharing program, but the other registrant(s) developing the data has refused to accept the offer. To qualify for this option, you must submit documentation to the Agency proving that you have made an offer to another registrant (who has an obligation to submit data) to share in the burden of developing that data. You must also submit to the Agency a completed EPA Form 8570-32, Certification of Offer to Cost Share in the Development of Data, Attachment 7. In addition, you must demonstrate that the other registrant to whom the offer was made has not accepted your offer to enter into a cost-sharing agreement by including a copy of your offer and proof of the other registrant's receipt of that offer (such as a certified mail receipt). Your offer must, in addition to anything else, offer to share in the burden of producing the data upon terms to be agreed to or, failing agreement, to be bound by binding arbitration as provided by FIFRA section 3(c)(2)(B)(iii) and must not qualify this offer. The other registrant must also inform EPA of its election of an option to develop and submit the data required by this Notice by submitting a Data Call-In Response Form and a Requirements Status and Registrant's Response Form committing to develop and submit the data required by this Notice.

In order for you to avoid suspension under this option, you may not withdraw your offer to share in the burden of developing the data. In addition, the other registrant must fulfill its commitment to develop and submit the data as required by this Notice. If the other registrant fails to develop the data or for some other reason is subject to suspension, your registration as well as that of the other registrant normally will be subject to initiation of suspension proceedings, unless you commit to submit, and do submit, the required data in the specified time frame. In such cases, the Agency generally will not grant a time extension for submitting the data.

Option 4. Submitting an Existing Study

If you choose to submit an existing study in response to this Notice, you must determine that the study satisfies the requirements imposed by this Notice. You may only submit a study that has not been previously submitted to the Agency or previously cited by anyone. Existing studies are studies which predate issuance of this Notice. Do not use this option if you are submitting data to upgrade a study. (See Option 5).

You should be aware that if the Agency determines that the study is not acceptable, the Agency will require you to comply with this Notice, normally without an extension of the required date of submission. The Agency may determine at any time that a study is not valid and needs to be repeated.

To meet the requirements of the DCI Notice for submitting an existing study, all of the following three criteria must be clearly Met:

a. You must certify at the time that the existing study is submitted that the raw data and specimens from the study are available for audit and review and you must identify where they are available. This must be done in accordance with the requirements of the Good Laboratory Practice (GLP) regulation, 40 CFR Part 160. As stated in 40 CFR 160.3 'Raw data' means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the exact copy or exact transcript may be substituted for the original source as raw data. 'Raw data' may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments." The term "specimens", according to 40 CFR 160.3, means "any material derived from a test system for examination or analysis."

b. Health and safety studies completed after May 1984 also must also contain all GLP-required quality assurance and quality control information, pursuant to the requirements of 40 CFR Part 160. Registrants also must certify at the time of submitting the existing study that such GLP information is available for post May 1984 studies by including an appropriate statement on or attached to the study signed by an authorized official or representative of the registrant.

c. You must certify that each study fulfills the acceptance criteria for the Guideline relevant to the study provided in the FIFRA Accelerated Reregistration Phase 3 Technical Guidance and that the study has been conducted according to the Pesticide Assessment Guidelines (PAG) or meets the purpose of the PAG (both available from NTIS). A study not conducted according to the PAG may be submitted to the Agency for consideration if the registrant believes that the study clearly meets the purpose of the PAG. The registrant is referred to 40 CFR 158.70 which states the Agency's policy regarding acceptable protocols. If you wish to submit the study, you must, in addition to certifying that the purposes of the PAG are met by the study, clearly articulate the rationale why you believe the study meets the purpose of the PAG, including copies of any supporting information or data. It has been the Agency's experience that studies completed prior to January 1970 rarely satisfied the purpose of the PAG and that necessary raw data usually are not available for such studies.

If you submit an existing study, you must certify that the study meets all requirements of the criteria outlined above.

If EPA has previously reviewed a protocol for a study you are submitting, you must identify any action taken by the Agency on the protocol and must indicate, as part of your certification, the manner in which all Agency comments, concerns, or issues were addressed in the final protocol and study.

If you know of a study pertaining to any requirement in this Notice which does not meet the criteria outlined above but does contain factual information regarding unreasonable adverse effects, you must notify the Agency of such a study. If such study is in the Agency's files, you need only cite it along with the notification. If not in the Agency's files, you must submit a summary and copies as required by PR Notice 86-5.

Option 5. Upgrading a Study

If a study has been classified as partially acceptable and upgradeable, you may submit data to upgrade that study. The Agency will review the data submitted and determine if the requirement is satisfied. If the Agency decides the requirement is not satisfied, you may still be required to submit new data normally without any time extension. Deficient, but upgradeable studies will normally be classified as supplemental. However, it is important to note that not all studies classified as supplemental are upgradeable. If you have questions regarding the classification of a study or whether a study may be upgraded, call or write the contact person listed in Attachment 1. If you submit data to upgrade an existing study you must satisfy or supply information to correct all deficiencies in the study identified by EPA. You must provide a clearly articulated rationale of how the deficiencies have been remedied or corrected and why the study should be rated as acceptable to EPA. Your submission must also specify the MRID number(s) of the study which you are attempting to upgrade and must be in conformance with PR Notice 86-5.

Do not submit additional data for the purpose of upgrading a study classified as unacceptable and determined by the Agency as not capable of being upgraded.

This option also should be used to cite data that has been previously submitted to upgrade a study, but has not yet been reviewed by the Agency. You must provide the MRID number of the data submission as well as the MRID number of the study being upgraded.

The criteria for submitting an existing study, as specified in Option 4 above, apply to all data submissions intended to upgrade studies. Additionally, your submission of data intended to upgrade studies must be accompanied by a certification that you comply with each of those criteria, as well as a certification regarding protocol compliance with Agency requirements.

Option 6. Citing Existing Studies

If you choose to cite a study that has been previously submitted to EPA, that study must have been previously classified by EPA as acceptable, or it must be a study which has not yet been reviewed by the Agency. Acceptable toxicology studies generally will have been classified as "core-guideline" or "core-minimum." For ecological effects studies, the classification generally would be a rating of "core." For all other disciplines the classification would be "acceptable." With respect to any studies for which you wish to select this option, you must provide the MRID number of the study you are citing and, if the study has been reviewed by the Agency, you must provide the Agency's classification of the study.

If you are citing a study of which you are not the original data submitter, you must submit a completed copy of EPA Form 8570-31, Certification with Respect to Data Compensation Requirements.

2. Product Specific Data

If you acknowledge on the product specific Data Call-In Response Form that you agree to satisfy the product specific data requirements (i.e. you select option 7a or 7b), then you must select one of the six options on the Requirements Status and Reqistrant's Response Form related to data production for each data requirement. Your option selection should be entered under item number 9, "Registrant Response." The six options related to data production are the first six options discussed under item 9 in the instructions for completing the Requirements Status and Registrant's Response Form. These six options are listed immediately below with information in parentheses to guide registrants to additional instructions provided in this Section. The options are:

(1) I will generate and submit data within the specified time-frame (Developing Data)
(2) I have entered into an agreement with one or more registrants to develop data jointly (Cost Sharing)
(3) I have made offers to cost-share (Offers to Cost Share)
(4) I am submitting an existing study that has not been submitted previously to the Agency by anyone (Submitting an Existing Study)
(5) I am submitting or citing data to upgrade a study classified by EPA as partially acceptable and upgradeable (Upgrading a Study)
(6) I am citing an existing study that EPA has classified as acceptable or an existing study that has been
submitted but not reviewed by the Agency (Citing an Existing Study)

Option 1. Developing Data -- The requirements for developing product specific data are the same as those described for generic data (see Section III.C.1, Option 1) except that normally no protocols or progress reports are required.

Option 2. Agree to Share in Cost to Develop Data -- If you enter into an agreement to cost share, the same requirements apply to product specific data as to generic data (see Section III.C.1, Option 2). However, registrants may only choose this option for acute toxicity data and certain efficacy data and only if EPA has indicated in the attached data tables that your product and at least one other product are similar for purposes of depending on
the same data. If this is the case, data may be generated for just one of the products in the group. The registration number of the product for which data will be submitted must be noted in the agreement to cost share by the registrant selecting this option.

Option 3. Offer to Share in the Cost of Data Development --The same requirements for generic data (Section III.C.I., Option 3) apply to this option. This option only applies to acute toxicity and certain efficacy data as described in option 2 above.

Option 4. Submitting an Existing Study -- The same requirements described for generic data (see Section III.C.1., Option 4) apply to this option for product specific data.

Option 5. Upgrading a Study -- The same requirements described for generic data (see Section III.C.1., Option 5) apply to this option for product specific data.

Option 6. Citing Existing Studies -- The same requirements described for generic data (see Section III.C.1., Option 6) apply to this option for product specific data.

Registrants who select one of the above 6 options must meet all of the requirements described in the instructions for completing the Data Call-In Response Form and the Requirements Status and Registrant's Response Form, and in the generic data requirements section (III.C.1.), as appropriate.

III-D REQUESTS FOR DATA WAIVERS

1. Generic Data

There are two types of data waiver responses to this Notice. The first is a request for a low volume/minor use waiver and the second is a waiver request based on your belief that the data requirement(s) are not appropriate for your product.

a. Low Volume/Minor Use Waiver

Option 8 under item 9 on the Requirements Status and Registrant's Response Form. Section 3(c)(2)(A) of FIFRA requires EPA to consider the appropriateness of requiring data for low volume, minor use pesticides. In implementing this provision, EPA considers low volume pesticides to be only those active ingredients whose total production volume for all pesticide registrants is small. In determining whether to grant a low volume, minor use waiver, the Agency will consider the extent, pattern and volume of use, the economic incentive to conduct the testing, the importance of the pesticide, and the exposure and risk from use of the pesticide. If an active ingredient is used for both high volume and low volume uses, a low volume exemption will not be approved. If all uses of an active ingredient are low volume and the combined volumes for all uses are also low, then an exemption may be granted, depending on review of other information outlined below. An exemption will not be granted if any registrant of the active ingredient elects to conduct the testing. Any registrant receiving a low volume minor use waiver must remain within the sales figures in their forecast supporting the waiver request in order to remain qualified for such waiver. If granted a waiver, a registrant will be required, as a condition of the waiver, to submit annual sales reports. The Agency will respond to requests for waivers in writing.

To apply for a low volume, minor use waiver, you must submit the following information, as applicable to your product(s), as part of your 90-day response to this Notice:

(i). Total company sales (pounds and dollars) of all registered product(s) containing the active ingredient. If applicable to the active ingredient, include foreign sales for those products that are not registered in this country but are applied to sugar (cane or beet), coffee, bananas, cocoa, and other such crops. Present the above information by year for each of the past five years.

(ii) Provide an estimate of the sales (pounds and dollars) of the active ingredient for each major use site. Present the above information by year for each of the past five years.

(iii) Total direct production cost of product(s) containing the active ingredient by year for the past five years. Include information on raw material cost, direct labor cost, advertising, sales and marketing, and any other significant costs listed separately.

(iv) Total indirect production cost (e.g. plant overhead, amortized plant and equipment) charged to product(s) containing the active ingredient by year for the past five years. Exclude all non-recurring costs that were directly related to the active ingredient, such as costs of initial registration and any data development.

(v) A list of each data requirement for which you seek a waiver. Indicate the type of waiver sought and the estimated cost to you (listed separately for each data requirement and associated test) of conducting the testing needed to fulfill each of these data requirements.

(vi) A list of each data requirement for which you are not seeking any waiver and the estimated cost to you (listed separately for each data requirement and associated test) of conducting the testing needed to fulfill each of these data requirements.

(vii) For each of the next ten years, a year-by-year forecast of company sales (pounds and dollars) of the active ingredient, direct production costs of product(s) containing the active ingredient (following the parameters in item 2 above), indirect production costs of product(s) containing the active ingredient (following the parameters in item 3 above), and costs of data development pertaining to the active ingredient.

(viii) A description of the importance and unique benefits of the active ingredient to users. Discuss the use patterns and the effectiveness of the active ingredient relative to registered alternative chemicals and non-chemical control strategies. Focus on benefits unique to the active ingredient, providing information that is as quantitative as possible. If you do not have quantitative data upon which to base your estimates, then present the reasoning used to derive your estimates. To assist the Agency in determining the degree of importance of the active ingredient in terms of its benefits, you should provide information on any of the following factors, as applicable to your product(s): (a) documentation of the usefulness of the active ingredient in Integrated Pest Management, (b) description of the beneficial impacts on the environment of use of the active ingredient, as opposed to its registered alternatives,

(c) information on the breakdown of the active ingredient after use and on its persistence in the environment, and (d) description of its usefulness against a pest(s) of public health significance.

Failure to submit sufficient information for the Agency to make a determination regarding a request for a low volume/minor use waiver will result in denial of the request for a waiver.

b. Request for Waiver of Data

Option 9, under Item 9, on the Requirements Status and Registrant's Response Form. This option may be used if you believe that a particular data requirement should not apply because the requirement is inappropriate. You must submit a rationale explaining why you believe the data requirements should not apply. You also must submit the current label(s) of your product(s) and, if a current copy of your Confidential Statement of Formula is not already on file you must submit a current copy.

You will be informed of the Agency's decision in writing. If the Agency determines that the data requirements of this Notice are not appropriate to your product(s), you will not be required to supply the data pursuant to section 3(c)(2)(B). If EPA determines that the data are required for your product(s), you must choose a method of meeting the requirements of this Notice within the time frame provided by this Notice. Within 30 days of your receipt of the Agency's written decision, you must submit a revised Requirements Status and Registrant's Response Form indicating the option chosen.

2. Product Specific Data

If you request a waiver for product specific data because you believe it is inappropriate, you must attach a complete justification for the request including technical reasons, data and references to relevant EPA regulations, guidelines or policies. (Note: any supplemental data must be submitted in the format required by PR Notice 86-5). This will be the only opportunity to state the reasons or provide information in support of your request. If the Agency approves your waiver request, you will not be required to supply the data pursuant to section 3(c)(2)(B) of FIFRA. If the Agency denies your waiver request, you must choose an option for meeting the data requirements of this Notice within 30 days of the receipt of the Agency's decision. You must indicate and submit the option chosen on the product specific Requirements Status and Registrant's Response Form. Product specific data requirements for product chemistry, acute toxicity and efficacy (where appropriate) are required for all products and the Agency would grant a waiver only under extraordinary circumstances. You should also be aware that submitting a waiver request will not automatically extend the due date for the study in question. Waiver requests submitted without adequate supporting rationale will be denied and the original due date will remain in force.

SECTION IV. CONSEQUENCES OF FAILURE TO COMPLY WITH THIS NOTICE

IV-A NOTICE OF INTENT TO SUSPEND

The Agency may issue a Notice of Intent to Suspend products subject to this Notice due to failure by a registrant to comply with the requirements of this Data Call-In Notice, pursuant to FIFRA section 3(c)(2)(B). Events which may be the basis for issuance of a Notice of Intent to Suspend include, but are not limited to, the following:

1. Failure to respond as required by this Notice within 90 days of your receipt of this Notice.

2. Failure to submit on the required schedule an acceptable proposed or final protocol when such is required to be submitted to the Agency for review.

3. Failure to submit on the required schedule an adequate progress report on a study as required by this Notice.

4. Failure to submit on the required schedule acceptable data as required by this Notice.

5. Failure to take a required action or submit adequate information pertaining to any option chosen to address the data requirements (e.g., any required action or information pertaining to submission or citation of existing studies or offers, arrangements, or arbitration on the sharing of costs or the formation of Task Forces, failure to comply with the terms of an agreement or arbitration concerning joint data development or failure to comply with any terms of a data waiver).

6. Failure to submit supportable certifications as to the conditions of submitted studies, as required by Section III-C of this Notice.

7. Withdrawal of an offer to share in the cost of developing required data.

8. Failure of the registrant to whom you have tendered an offer to share in the cost of developing data and provided proof of the registrant's receipt of such offer or failure of a registrant on whom you rely for a generic data exemption either to:

   i. Inform EPA of intent to develop and submit the data required by this Notice on a Data Call-In Response Form and a Requirements Status and Reqistrant's Response Form.

   ii. Fulfill the commitment to develop and submit the data as required by this Notice; or

iii. Otherwise take appropriate steps to meet the requirements stated in this Notice,

unless you commit to submit and do submit the required data in the specified time frame.

9. Failure to take any required or appropriate steps, not mentioned above, at any time following the issuance of this Notice.

IV-B. BASIS FOR DETERMINATION THAT SUBMITTED STUDY IS UNACCEPTABLE

The Agency may determine that a study (even if submitted within the required time) is unacceptable and constitutes a basis for issuance of a Notice of Intent to Suspend. The grounds for suspension include, but are not limited to, failure to meet any of the following:

1) EPA requirements specified in the Data Call-In Notice or other documents incorporated by reference (including, as applicable, EPA Pesticide Assessment Guidelines, Data Reporting Guidelines, and GeneTox Health Effects Test Guidelines) regarding the design, conduct, and reporting of required studies. Such requirements include, but are not limited to, those relating to test material, test procedures, selection of species, number of animals, sex and distribution of animals, dose and effect levels to be tested or attained, duration of test, and, as applicable, Good Laboratory Practices.

2) EPA requirements regarding the submission of protocols, including the incorporation of any changes required by the Agency following review.

3) EPA requirements regarding the reporting of data, including the manner of reporting, the completeness of results, and the adequacy of any required supporting (or raw) data, including, but not limited to, requirements referenced or included in this Notice or contained in PR 86-5. All studies must be submitted in the form of a final report; a preliminary report will not be considered to fulfill the submission requirement.

IV-C EXISTING STOCKS OF SUSPENDED OR CANCELLED PRODUCTS

EPA has statutory authority to permit continued sale, distribution and use of existing stocks of a pesticide product which has been suspended or cancelled if doing so would be consistent with the purposes of the Act.

The Agency has determined that such disposition by registrants of existing stocks for a suspended registration when a section 3(c)(2)(B) data request is outstanding generally would not be consistent with the Act's purposes. Accordingly, the Agency anticipates granting registrants permission to sell, distribute, or use existing stocks of suspended product(s) only in exceptional circumstances. If you believe such disposition of existing stocks of your product(s) which may be suspended for failure to comply with this Notice should be permitted, you have

the burden of clearly demonstrating to EPA that granting such permission would be consistent with the Act. You also must explain why an "existing stocks" provision is necessary, including a statement of the quantity of existing stocks and your estimate of the time required for their sale, distribution, and use. Unless you meet this burden, the Agency will not consider any request pertaining to the continued sale, distribution, or use of your existing stocks after suspension.

If you request a voluntary cancellation of your product(s) as a response to this Notice and your product is in full compliance with all Agency requirements, you will have, under most circumstances, one year from the date your 90 day response to this Notice is due, to sell, distribute, or use existing stocks. Normally, the Agency will allow persons other than the registrant such as independent distributors, retailers and end users to sell, distribute or use such existing stocks until the stocks are exhausted. Any sale, distribution or use of stocks of voluntarily cancelled products containing an active ingredient for which the Agency has particular risk concerns will be determined on a case-by-case basis.

Requests for voluntary cancellation received after the 90 day response period required by this Notice will not result in the agency granting any additional time to sell, distribute, or use existing stocks beyond a year from the date the 90 day response was due, unless you demonstrate to the Agency that you are in full compliance with all Agency requirements, including the requirements of this Notice. For example, if you decide to voluntarily cancel your registration six months before a 3-year study is scheduled to be submitted, all progress reports and other information necessary to establish that you have been conducting the study in an acceptable and good faith manner must have been submitted to the Agency, before EPA will consider granting an existing stocks provision.

SECTION V. REGISTRANTS' OBLIGATION TO REPORT POSSIBLE UNREASONABLE ADVERSE EFFECTS

Registrants are reminded that FIFRA section 6(a)(2) states that if at any time after a pesticide is registered a registrant has additional factual information regarding unreasonable adverse effects on the environment by the pesticide, the registrant shall submit the information to the Agency. Registrants must notify the Agency of any factual information they have, from whatever source, including but not limited to interim or preliminary results of studies, regarding unreasonable adverse effects on man or the environment. This requirement continues as long as the products are registered by the Agency.

SECTION VI. INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding the requirements and procedures established by this Notice, call the contact person(s) listed in Attachment 1, the Data Call-In Chemical Status Sheet.

All responses to this Notice must include completed Data Call-In Response Forms (Attachment 2)and completed Requirements Status and Registrant's Response Forms (Attachment 3), for both (generic and product specific data) and any other documents required by this Notice, and should be submitted to the contact person(s) identified in Attachment 1. If the voluntary cancellation or generic data exemption option is chosen, only the Generic and Product Specific Data Call-In Response Forms need be submitted.

The Office of Compliance (OC) of the Office of Enforcement and Compliance Assurance (OECA), EPA, will be monitoring the data being generated in response to this Notice.

Sincerely yours,

Lois A. Rossi, Director
Special Review and
Reregistration Division

Attachments

The Attachments to this Notice are:

1 - Data Call-In Chemical Status Sheet
2 - Generic Data Call-In and Product Specific Data Call-In Response Forms with Instructions
3 - Generic Data Call-In and Product Specific Data Call-In Requirements Status and Registrant's Response Forms with Instructions
4 - EPA Batching of End-Use Products for Meeting Acute Toxicology Data Requirements for Reregistration
5 - List of Registrants Receiving This Notice
6 - Confidential Statement of Formula, Cost Share and Data Compensation Forms

DIPHENYLAMINE DATA CALL-IN CHEMICAL STATUS SHEET

INTRODUCTION

You have been sent this Product Specific Data Call-In Notice because you have product(s) containing diphenylamine.

This Product Specific Data Call-In Chemical Status Sheet, contains an overview of data required by this notice, and point of contact for inquiries pertaining to the reregistration of diphenylamine. This attachment is to be used in conjunction with (1) the Product Specific Data Call-In Notice, (2) the Product Specific Data Call-In Response Form (Attachment 2), (3) the Requirements Status and Registrant's Form (Attachment 3), (4) EPA's Grouping of End-Use Products for Meeting Acute Toxicology Data Requirement (Attachment 4), (5) the EPA Acceptance Criteria (Attachment 5), (6) a list of registrants receiving this DCI (Attachment 6) and (7) the Cost Share and Data Compensation Forms in replying to this diphenylamine Product Specific Data Call-In (Attachment 7). Instructions and guidance accompany each form.

DATA REQUIRED BY THIS NOTICE

The additional data requirements needed to complete the database for diphenylamine are contained in the Requirements Status and Registrant's Response, Attachment 3. The Agency has concluded that additional data on diphenylamine are needed for specific products. These data are required to be submitted to the Agency within the time frame listed. These data are needed to fully complete the reregistration of all eligible diphenylamine products.

INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding this product specific data requirements and procedures established by this Notice, please contact CP Moran at (703) 308-8590.

All responses to this Notice for the Product Specific data requirements should be submitted to:

CP Moran
Chemical Review Manager Team 81
Product Reregistration Branch
Special Review and Reregistration Branch 7508W
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, D.C. 20460

RE: **2665**

2665 DATA CALL-IN CHEMICAL STATUS SHEET

INTRODUCTION

You have been sent this Generic Data Call-In Notice because you have product(s) containing diphenylamine.

This Generic Data Call-In Chemical Status Sheet, contains an overview of data required by this notice, and point of contact for inquiries pertaining to the reregistration of diphenylamine. This attachment is to be used in conjunction with (1) the Generic Data Call-In Notice, (2) the Generic Data Call-In Response Form (Attachment 2), (3) the Requirements Status and Registrant's Form (Attachment 2), (4) a list of registrants receiving this DCI (Attachment 4), (5) the EPA Acceptance Criteria (Attachment 5), and (6) the Cost Share and Data Compensation Forms in replying to this diphenylamine Generic Data Call In (Attachment F). Instructions and guidance accompany each form.

DATA REQUIRED BY THIS NOTICE

The additional data requirements needed to complete the generic database for diphenylamine are contained in the Requirements Status and Registrant's Response, Attachment C. The Agency has concluded that additional product chemistry data on diphenylamine are needed. These data are needed to fully complete the reregistration of all eligible diphenylamine products.

INQUIRIES AND RESPONSES TO THIS NOTICE

If you have any questions regarding the generic data requirements and procedures established by this Notice, please contact Dennis Deziel at (703) 308-8180.

All responsades to this Notice for the generic data requirements should be submitted to:

Dennis Deziel, Chemical Review Manager
Reregistration Branch I
Special Review and Registration Division (H7508W)
Office of Pesticiafde Programs
U.S. Environmental Protection Agency
Washington, D.C. 20460
RE: 2665

Instructions For Completing The "Data Call-In Response Forms" For The Generic And Product Specific Data Call-In

INTRODUCTION

These instructions apply to the Generic and Product Specific "Data Call-In Response Forms" and are to be used by registrants to respond to generic and product specific Data Call-Ins as part of EPA's Reregistration Program under the Federal Insecticide, Fungicide, and Rodenticide Act. If you are an end-use product registrant only and have been sent this DCI letter as part of a RED document you have been sent just the product specific "Data Call-In Response Forms." Only registrants responsible for generic data have been sent the generic data response form. **The type of Data Call-In (generic or product specific) is indicated in item number 3 ("Date and Type of DCI") on each form.**

Although the form is the same for both generic and product specific data, instructions for completing these forms are different. Please read these instructions carefully before filling out the forms.

EPA has developed these forms individually for each registrant, and has preprinted these forms with a number of items. DO NOT use these forms for any other active ingredient.

Items 1 through 4 have been preprinted on the form. Items 5 through 7 must be completed by the registrant as appropriate. Items 8 through 11 must be completed by the registrant before submitting a response to the Agency.

The public reporting burden for this collection of information is estimated to average 15 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, Mail Code 2136, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, D.C. 20460; and to the Office of Management and Budget, Paperwork Reduction Project 2070-0107, Washington, D.C. 20503.

INSTRUCTIONS FOR COMPLETING THE DATA CALL-IN RESPONSE FORMS
Generic and Product Specific Data Call-In

Item 1. **ON BOTH FORMS**: This item identifies your company name, number and address.

Item 2. **ON BOTH FORMS:** This item identifies the case number, case name, EPA chemical number and chemical name.

Item 3. **ON BOTH FORMS:** This item identifies the type of Data Call-In. The date of issuance is date stamped.

Item 4. **ON BOTH FORMS:** This item identifies the EPA product registrations relevant to the data call-in. Please note that you are also responsible for informing the Agency of your response regarding any product that you believe may be covered by this Data Call-In but that is not listed by the Agency in Item 4. You must bring any such apparent omission to the Agency's attention within the period required for submission of this response form.

Item 5. **ON BOTH FORMS:** Check this item for each product registration you wish to cancel voluntarily. If a registration number is listed for a product for which you previously requested voluntary cancellation, indicate in Item 5 the date of that request. Since this Data Call-In requires both generic and product specific data, you must complete item 5 on both Data Call-In response forms. You do not need to complete any item on the Requirements Status and Registrant's Response Forms.

Item 6a. **ON THE GENERIC DATA FORM:** Check this Item if the Data Call-In is for generic data as indicated in Item 3 and you are eligible for a Generic Data Exemption for the chemical listed in Item 2 and used in the subject product. By electing this exemption, you agree to the terms and conditions of a Generic Data Exemption as explained in the Data Call-In Notice.

If you are eligible for or claim a Generic Data Exemption, enter the EPA registration Number of each registered source of that active ingredient that you use in your product.

Typically, if you purchase an EPA-registered product from one or more other producers (who, with respect to the incorporated product, are in compliance with this and any other outstanding Data Call-In Notice), and incorporate that product into all your products, you may complete this item for all products listed on this form. If, however, you produce the active ingredient yourself, or use any unregistered product (regardless of the fact that some of your sources

are registered), you may not claim a Generic Data Exemption and you may not select this item.

INSTRUCTIONS FOR COMPLETING THE DATA CALL-IN RESPONSE FORMS
Generic and Product Specific Data Call-In

Item 6b. **ON THE GENERIC DATA FORM:** Check this Item if the Data Call-In is for generic data as indicated in Item 3 and if you are agreeing to satisfy the generic data requirements of this Data Call-In. Attach the Requirements Status and Registrant's Response Form that indicates how you will satisfy those requirements.

NOTE: **Item 6a and 6b are not applicable for Product Specific Data.**

Item 7a. **ON THE PRODUCT SPECIFIC DATA FORM:** For each manufacturing use product (MUP) for which you wish to maintain registration, you must agree to satisfy the data requirements by responding "yes."

Item 7b. For each end use product (EUP) for which you wish to maintain registration, you must agree to satisfy the data requirements by responding "yes."

FOR BOTH MUP and EUP products

You should also respond "yes" to this item (7a for MUP's and 7b for EUP's) if your product is identical to another product and you qualify for a data exemption. You must provide the EPA registration numbers of your source(s); do not complete the Requirements Status and Registrant's Response form. Examples of such products include repackaged products and Special Local Needs (Section 24c) products which are identical to federally registered products.

If you are requesting a data waiver, answer "yes" here; in addition, on the "Requirements Status and Registrant's Response" form under Item 9, you must respond with option 7 (Waiver Request) for each study for which you are requesting a waiver.

NOTE: **Item 7a and 7b are not applicable for Generic Data.**

Item 8. **ON BOTH FORMS:** This certification statement must be signed by an authorized representative of your company and the person signing must include his/her title. Additional pages used in your response must be initialled and dated in the space provided for the certification.

Item 9. **ON BOTH FORMS:** Enter the date of signature.

Item 10. **ON BOTH FORMS:** Enter the name of the person EPA should contact with questions regarding your response.

Item 11. **ON BOTH FORMS:** Enter the phone number of your company contact.

Note: You may provide additional information that does not fit on this form in a signed letter that accompanies your response. For example, you may wish to report that your product has already been transferred to another company or that you have already voluntarily cancelled this product. For these cases, please supply all relevant details so that EPA can ensure that its records are correct.

Instructions For Completing The "Requirements Status and Registrant's Response Forms" For The Generic and Product Specific Data Call-In

INTRODUCTION

These instructions apply to the Generic and Product Specific "Requirements Status and Registrant's Response Forms" and are to be used by registrants to respond to generic and product specific Data Call-In's as part of EPA's reregistration program under the Federal Insecticide, Fungicide, and Rodenticide Act. If you are an end-use product registrant only and have been sent this DCI letter as part of a RED document you have been sent just the product specific "Requirements Status and Registrant's Response Forms." Only registrants responsible for generic data have been sent the generic data response forms. **The type of Data Call-In (generic or product specific) is indicated in item number 3 ("Date and Type of DCI") on each form.**

Although the form is the same for both product specific and generic data, instructions for completing the forms differ slightly. Specifically, options for satisfying product specific data requirements do not include (1) deletion of uses or (2) request for a low volume/minor use waiver. Please read these instructions carefully before filling out the forms.

EPA has developed these forms individually for each registrant, and has preprinted these forms to include certain information unique to this chemical. DO NOT use these forms for any other active ingredient.

Items 1 through 8 have been preprinted on the form. Item 9 must be completed by the registrant as appropriate. Items 10 through 13 must be completed by the registrant before submitting a response to the Agency.

The public reporting burden for this collection of information is estimated to average 30 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, Mail Code 2136, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, D.C. 20460; and to the Office of Management and Budget, Paperwork Reduction Project 2070-0107, Washington, D.C. 20503.

INSTRUCTIONS FOR COMPLETING THE "REQUIREMENTS STATUS AND REGISTRANT'S RESPONSE FORMS"

Generic and Product Specific Data Call-In

Item 1. **ON BOTH FORMS:** This item identifies your company name, number and address.

Item 2. **ON THE GENERIC DATA FORM:** This item identifies the case number, case name, EPA chemical number and chemical name.

ON THE PRODUCT SPECIFIC DATA FORM: This item identifies the case number, case name, and the EPA Registration Number of the product for which the Agency is requesting product specific data.

Item 3. **ON THE GENERIC DATA FORM:** This item identifies the type of Data Call-In. The date of issuance is date stamped.

ON THE PRODUCT SPECIFIC DATA FORM: This item identifies the type of Data Call-In. The date of issuance is also date stamped. Note the unique identifier number (ID#) assigned by the Agency. This ID number must be used in the transmittal document for any data submissions in response to this Data Call-In Notice.

Item 4. **ON BOTH FORMS:** This item identifies the guideline reference number of studies required. These guidelines, in addition to the requirements specified in the Data Call-In Notice, govern the conduct of the required studies. Note that series 61 and 62 in product chemistry are now listed under 40 CFR 158.155 through 158.180, Subpart c.

Item 5. **ON BOTH FORMS:** This item identifies the study title associated with the guideline reference number and whether protocols and 1, 2, or 3-year progress reports are required to be submitted in connection with the study. As noted in Section III of the Data Call-In Notice, 90-day progress reports are required for all studies.

If an asterisk appears in Item 5, EPA has attached information relevant to this guideline reference number to the Requirements Status and Reqistrant's Response Form.

INSTRUCTIONS FOR COMPLETING THE "REQUIREMENTS STATUS AND REGISTRANT'S RESPONSE FORMS"

Generic and Product Specific Data Call-In

Item 6. **ON BOTH FORMS:** This item identifies the code associated with the use pattern of the pesticide. In the case of efficacy data (product specific requirement), the required study only pertains to products which have the use sites and/or pests indicated. A brief description of each code follows:

A	Terrestrial food
B	Terrestrial feed
C	Terrestrial non-food
D	Aquatic food
E	Aquatic non-food outdoor
F	Aquatic non-food industrial
G	Aquatic non-food residential
H	Greenhouse food
I	Greenhouse non-food crop
J	Forestry
K	Residential
L	Indoor food
M	Indoor non-food
N	Indoor medical
O	Indoor residential

Item 7. **ON BOTH FORMS:** This item identifies the code assigned to the substance that must be used for testing. A brief description of each code follows:

EUP	End-Use Product
MP	Manufacturing-Use Product
MP/TGAI	Manufacturing-Use Product and Technical Grade Active Ingredient
PAI	Pure Active Ingredient
PAI/M	Pure Active Ingredient and Metabolites
PAI/PAIRA	Pure Active Indredient or Pute Active Ingredient Radiolabelled
PAIRA	Pure Active Ingredient Radiolabelled
PAIRA/M	Pure Active Ingredient Radiolabelled and Metabolites
PAIRA/PM	Pure Active Ingredient Radiolabelled and Plant Metabolites
TEP	Typical End-Use Product
TEP ___%	Typical End-Use Product, Percent Active Ingredient Specified
TEP/MET	Typical End-Use Product and Metabolites

TEP/PAI/M	Typical End-Use Product or Pure Active Ingredient and Metabolites
TGAI	Technical Grade Active Ingredient
TGAI/PAI	Technical Grade Active Ingredient or Pure Active Ingredient
TGAI/PAIRA	Technical Grade Active Ingredient or Pure Active Ingredient Radiolabelled
TGAI/TEP	Technical Grade Active Ingredient or Typical End-Use Product
MET	Metabolites
IMP	Impurities
DEGR	Degradates
*	See: guideline comment

Item 8. This item completed by the Agency identifies the time frame allowed for submission of the study or protocol identified in item 5.

ON THE GENERIC DATA FORM: The time frame runs from the date of your receipt of the Data Call-In notice.

ON THE PRODUCT SPECIFIC DATA FORM: The due date for submission of product specific studies begins from the date stamped on the letter transmitting the Reregistration Eligibility Decision document, and not from the date of receipt. However, your response to the Data Call-In itself is due 90 days from the date of receipt.

Item 9. **ON BOTH FORMS:** Enter the appropriate Response Code or Codes to show how you intend to comply with each data requirement. Brief descriptions of each code follow. The Data Call-In Notice contains a fuller description of each of these options.

Option 1. **ON BOTH FORMS:** (Developing Data) I will conduct a new study and submit it within the time frames specified in item 8 above. By indicating that I have chosen this option, I certify that I will comply with all the requirements pertaining to the conditions for submittal of this study as outlined in the Data Call-In Notice and that I will provide the protocols and progress reports required in item 5 above.

Option 2. **ON BOTH FORMS:** (Agreement to Cost Share) I have entered into an agreement with one or more registrants to develop data jointly. By indicating that I have chosen this option, I certify that I will comply with all the requirements pertaining to sharing in the cost of developing data as outlined in the Data Call-In Notice.

However, for Product Specific Data, I understand that this option is available for acute toxicity or certain efficacy data **ONLY** if the Agency indicates in an attachment to this notice that my product is similar enough to another product to qualify for this option. I certify that another party in the agreement is committing to submit or provide the required data; if the required study is not submitted on time, my product may be subject to suspension.

Option 3. **ON BOTH FORMS:** (Offer to Cost Share) I have made an offer to enter into an agreement with one or more registrants to develop data jointly. I am also submitting a completed "Certification of offer to Cost Share in the Development of Data" form. I am submitting evidence that I have made an offer to another registrant (who has an obligation to submit data) to share in the cost of that data. I am including a copy of my offer and proof of the other registrant's receipt of that offer. I am identifying the party which is committing to submit or provide the required data; if the required study is not submitted on time, my product may be subject to suspension. I understand that other terms under Option 3 in the Data Call-In Notice apply as well.

However, for Product Specific Data, I understand that this option is available only for acute toxicity or certain efficacy data and only if the Agency indicates in an attachment to this Data Call-In Notice that my product is similar enough to another product to qualify for this option.

Option 4. **ON BOTH FORMS:** (Submitting Existing Data) I will submit an existing study by the specified due date that has never before been submitted to EPA. By indicating that I have chosen this option, I certify that this study meets all the requirements pertaining to the conditions for submittal of existing data outlined in the Data Call-In Notice and I have attached the needed supporting information along with this response.

Option 5. **ON BOTH FORMS:** (Upgrading a Study) I will submit by the specified due date, or will cite data to upgrade a study that EPA has classified as partially acceptable and potentially upgradeable. By indicating that I have chosen this option, I certify that I have met all the requirements pertaining to the conditions for submitting or citing existing data to upgrade a study described in the Data Call-In Notice. I am indicating on attached correspondence the Master Record Identification Number (MRID) that EPA has assigned to the data that I am citing as well as the MRID of the study I am attempting to upgrade.

Option 6. **ON BOTH FORMS:** (Citing a Study) I am citing an existing study that has been previously classified by EPA as acceptable, core, core

minimum, or a study that has not yet been reviewed by the Agency. If reviewed, I am providing the Agency's classification of the study.

However, for Product Specific Data, I am citing another registrant's study. I understand that this option is available **ONLY** for acute toxicity or certain efficacy data and **ONLY** if the cited study was conducted on my product, an identical product or a product which the Agency has "grouped" with one or more other products for purposes of depending on the same data. I may also choose this option if I am citing my own data. In either case, I will provide the MRID or Accession number (s). If I cite another registrant's data, I will submit a completed "Certification With Respect To Data Compensation Requirements" form.

FOR THE GENERIC DATA FORM ONLY: The following three options (Numbers 7, 8, and 9) are responses that apply only to the "Requirements Status and Registrant's Response Form" for generic data.

Option 7. (Deleting Uses) I am attaching an application for amendment to my registration deleting the uses for which the data are required.

Option 8. (Low Volume/Minor Use Waiver Request) I have read the statements concerning low volume-minor use data waivers in the Data Call-In Notice and I request a low-volume minor use waiver of the data requirement. I am attaching a detailed justification to support this waiver request including, among other things, all information required to support the request. I understand that, unless modified by the Agency in writing, the data requirement as stated in the Notice governs.

Option 9. (Request for Waiver of Data) I have read the statements concerning data waivers other than lowvolume minor-use data waivers in the Data Call-In Notice and I request a waiver of the data requirement. I am attaching a rationale explaining why I believe the data requirements do not apply. I am also submitting a copy of my current labels. (You must also submit a copy of your Confidential Statement of Formula if not already on file with EPA). I understand that, unless modified by the Agency in writing, the data requirement as stated in the Notice governs.

FOR PRODUCT SPECIFIC DATA: The following option (number 7) is a response that applies to the "Requirements Status and Registrant's Response Form" for product specific data.

Option 7. (Waiver Request) I request a waiver for this study because it is inappropriate for my product. I am attaching a complete justification for this request, including technical reasons, data and references to relevant

EPA regulations, guidelines or policies. [Note: any supplemental data must be submitted in the format required by P.R. Notice 86-5]. I understand that this is my only opportunity to state the reasons or provide information in support of my request. If the Agency approves my waiver request, I will not be required to supply the data pursuant to Section 3(c) (2) (B) of FIFRA. If the Agency denies my waiver request, I must choose a method of meeting the data requirements of this Notice by the due date stated by this Notice. In this case, I must, within 30 days-of my receipt of the Agency's written decision, submit a revised "Requirements Status" form specifying the option chosen. I also understand that the deadline for submission of data as specified by the original Data Call-In notice will not change.

Item 10. **ON BOTH FORMS:** This item must be signed by an authorized representative of your company. The person signing must include his/her title, and must initial and date all other pages of this form.

Item 11. **ON BOTH FORMS:** Enter the date of signature.

Item 12. **ON BOTH FORMS:** Enter the name of the person EPA should contact with questions regarding your response.

Item 13. **ON BOTH FORMS:** Enter the phone number of your company contact.

NOTE: You may provide additional information that does not fit on this form in a signed letter that accompanies this your response. For example, you may wish to report that your product has already been transferred to another company or that you have already voluntarily cancelled this

TRB'S BATCHING OF PRODUCTS CONTAINING DIPHENYLAMINE AS THE ACTIVE INGREDIENT FOR MEETING ACUTE TOXICITY DATA REQUIREMENTS FOR REREGISTRATION

In an effort to reduce the time, resources and number of animals needed to fulfill the acute toxicity data requirements for reregistration of products containing diphenylamine as the active ingredient, the Agency has batched products which can be considered similar for purposes of acute toxicity. Factors considered in the sorting process include each product's active and inert ingredients (identity, percent composition and biological activity), type of formulation (e.g., emulsifiable concentrate, aerosol, wettable powder, granular, etc.), and labeling (e.g., signal word, use classification, precautionary labeling, etc.). Note that the Agency is not describing batched products as "substantially similar" since some products within a batch may not be considered chemically similar or have identical use patterns.

Using available information, batching has been accomplished by the process described in the preceding paragraph. Notwith-standing the batching process, the Agency reserves the right to require, at any time, acute toxicity data for an individual product should the need arise.

Registrants of products within a batch may choose to cooperatively generate, submit or cite a single battery of six acute toxicological studies to represent all the products within that batch. It is the registrants' option to participate in the process with all other registrants, only some of the other registrants, or only their own products within a batch, or to generate all the required acute toxicological studies for each of their own products. If a registrant chooses to generate the data for a batch, he/she must use one of the products within the batch as the test material. If a registrant chooses to rely upon previously submitted acute toxicity data, he/she may do so provided that the data base is complete and valid by today's standards (see acceptance criteria attached), the formulation tested is considered by EPA to be similar for acute toxicity, and the formulation has not been significantly altered since submission and acceptance of the acute toxicity data. Regardless of whether new data is generated or existing data is referenced, registrants must clearly identify the test material by EPA Registration Number. If more than one confidential statement of formula (CSF) exists for a product, the registrant must indicate the formulation actually tested by identifying the corresponding CSF.

In deciding how to meet the product specific data requirements, registrants must follow the directions given in the Data Call-In Notice and its attachments appended to the RED. The DCI Notice contains two response forms which are to be completed and submitted to the Agency within 90 days of receipt. The first form, "Data Call-In Response," asks whether the registrant will meet the data requirements for each product. The second form, "Requirements Status and Registrant's Response," lists the product specific data required for each product, including the standard six acute toxicity tests. A registrant who wishes to participate in a batch must decide whether he/she will provide the data or depend on someone else to do so. If a registrant supplies the data to support a batch of products, he/she must select one of the following options: Developing Data (Option 1), Submitting an Existing Study (Option 4), Upgrading an Existing Study (Option 5) or Citing an Existing Study (Option 6). If a registrant depends on another's data, he/she must choose among: Cost Sharing (Option 2), Offers to Cost Share (Option 3) or Citing an Existing Study

(Option 6). If a registrant does not want to participate in a batch, the choices are Options 1, 4, 5 or 6. However, a registrant should know that choosing not to participate in a batch does not preclude other registrants in the batch from citing his/her studies and offering to cost share (Option 3) those studies.

Three products were found which contain diphenylamine as the active ingredient. All three products have been placed into the "no batch" category based on the active/inert ingredients and type of formulation. However, with the exception of eye and skin irritation data, EPA Reg. Nos. 2792-45 and 64864-3 may be supported by acute toxicity data performed with the technical [EPA Reg. No. 2792-47]. Eye and skin irritation data performed with EPA Reg. Nos. 2792-45 and 64864-3 [separately] are needed to support reregistration of these two products. Furthermore, since the Agency has obtained Material Safety Data Sheets which designate diphenylamine as a dermal sensitizer, dermal sensitization data are not required for any of these products. Each product, however, will be required to include a label statement indicating that the product may cause dermal sensitization following repeated exposure.

At a minimum, the acute data cited or submitted to support these products should meet the acceptance criteria included in this document. In addition, the acute toxicity values for diphenylamine [also included in this document] are for informational purposes only, and the data supporting these values may or may not meet the acceptance criteria.

No Batch	EPA Reg. No.	% Active Ingredient	Formulation Type
	2792-45	31.0	Liquid
	2792-47	99.9	Solid
	64864-3	15.0	Liquid

The following is a list of available documents for diphenylamine that may further assist you in responding to this Reregistration Eligibility Decision document. These documents may be obtained by the following methods:

Electronic
File format: Portable Document Format (.PDF) Requires Adobe® Acrobat or compatible reader. Electronic copies can be downloaded from the Pesticide Special Review and Reregistration Information System at 703-308-7224. They also are available on the Internet on EPA's gopher server using WWW (World Wide Web) on WWW.EPA.GOV., or contact CP Moran at (703)-308-8590.

1. PR Notice 86-5.

2. PR Notice 91-2 (pertains to the Label Ingredient Statement).

3. A full copy of this RED document.

4. A copy of the fact sheet for diphenylamine.

The following documents are part of the Administrative Record for diphenylamine and may included in the EPA's Office of Pesticide Programs Public Docket. Copies of these documents are not available electronically, but may be obtained by contacting the person listed on the Chemical Status Sheet.

1. Health and Environmental Effects Science Chapters.

2. Detailed Label Usage Information System (LUIS) Report.

The following Agency reference documents are not available electronically, but may be obtained by contacting the person listed on the Chemical Status Sheet of this RED document.

1. The Label Review Manual.

2. EPA Acceptance Criteria

Attachment 1. List of All Registrants Sent This Data Call-In (insert) Notice

Instructions for Completing the Confidential Statement of Formula

The Confidential Statement of Formula (CSF) Form 8570-4 must be used. Two legible, signed copies of the form are required. Following are basic instructions:

a. All the blocks on the form must be filled in and answered completely.

b. If any block is not applicable, mark it N/A.

c. The CSF must be signed, dated and the telephone number of the responsible party must be provided.

d. All applicable information which is on the product specific data submission must also be reported on the CSF.

e. All weights reported under item 7 must be in pounds per gallon for liquids and pounds per cubic feet for solids.

f. Flashpoint must be in degrees Fahrenheit and flame extension in inches.

g. For all active ingredients, the EPA Registration Numbers for the currently registered source products must be reported under column 12.

h. The Chemical Abstracts Service (CAS) Numbers for all actives and inerts and all common names for the trade names must be reported.

i. For the active ingredients, the percent purity of the source products must be reported under column 10 and must be exactly the same as on the source product's label.

j. All the weights in columns 13.a. and 13.b. must be in pounds, kilograms, or grams. In no case will volumes be accepted. Do not mix English and metric system units (i.e., pounds and kilograms).

k. All the items under column 13.b. must total 100 percent.

1. All items under columns 14.a. and 14.b. for the active ingredients must represent pure active form.

m. The upper and lower certified limits for ail active and inert ingredients must follow the 40 CFR 158.175 instructions. An explanation must be provided if the proposed limits are different than standard certified limits.

n. When new CSFs are submitted and approved, all previously submitted CSFs become obsolete for that specific formulation.

Confidential Business Information: Does Not Contain National Security Information (E.O. 12065) Form Approved. OMB No. 2070-0060. Approval Expires 2/28/94

EPA

United States Environmental Protection Agency
Office of Pesticide Programs (TS-767)
Washington, DC 20460

Confidential Statement of Formula

A. ☐ Basic Formulation ☐ Alternate Formulation

B. Page of

See Instructions on Back

1. Name and Address of Applicant/Registrant *(Include ZIP Code)*

2. Name and Address of Producer *(Include ZIP Code)*

3. Product Name

4. Registration No./File Symbol

5. EPA Product Mgr/Team No.

6. Country Where Formulated

7. Pounds/Gal or Bulk Density

8. pH

9. Flash Point/Flame Extension

EPA USE ONLY	10. Components in Formulation *(List as actually introduced into the formulation. Give commonly accepted chemical name, trade name, and CAS number.)*	11. Supplier Name & Address	12. EPA Reg. No.	13. Each Component in Formulation a. Amount	13. b. % by Weight	14. Certified Limits % by Weight a. Upper Limit	14. b. Lower Limit	15. Purpose in Formulation

16. Typed Name of Approving Official

17. Total Weight 100%

18. Signature of Approving Official

19. Title

20. Phone No. *(Include Area Code)*

21. Date

EPA Form 8570-4 (Rev. 12-90) **Previous editions are obsolete.** If you can photocopy this, please submit an additional copy. White - EPA File Copy (original) Yellow - Applicant copy

United States Environmental Protection Agency
Washington, D.C. 20460

Certification of Offer to Cost Share in the Development of Data

Form Approved OMB No. 2070-0106, 2070-0057 Approval Expires 3-31-99

Public reporting burden for this collection of information is estimated to average 15 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to, Chief Information Policy Branch, PM-233, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0106), Washington, DC 20503.

Please fill in blanks below:

Company Name	**Company Number**

Product Name	**EPA Reg. No.**

I Certify that:

My company is willing to develop and submit the data required by EPA under the authority of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), if necessary. However my company would prefer to enter into an agreement with one or more registrants to develop jointly or share in the cost of developingdata.

My firm has offered in writing to enter into such an agreement. That offer was irrevocable and included an offer to be bound by arbitration decision under section 3(c)(2)(B)(iii) of FIFRA if final agreement on all terms could not be reached otherwise. This offer was made to the following firms on the following date(s):

Name of Firm(s)	**Date of Offer**

Certification:

I certify that I am duly authorized to represent the company named above, and that the statements that I have made on this form and all attachments therein are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature of Company's Authorized Representative	**Date**

Name and Title (Please Type or Print)

EPA Form 8570-32 (5/91) Replaces EPA form 8580 which is obselete

United States Environmental Protection Agency
Washington, DC 20460

Form Approved
OMB No. 2070-0107, 2070-0057
Approval Expires 3-31-99

CERTIFICATION WITH RESPECT TO DATA COMPENSATION REQUIREMENTS

Public reporting burden for this collection of information is estimated to average 15 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to, Chief Information Policy Branch, PM-233, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0106), Washington, DC 20503.

Please fill in blanks below.

Company Name	Company Number

Product Name	EPA Reg. No.

I Certify that:

1. For each study cited in support of registration or reregistratiion under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) that is an exclusive use study, I am the original data submitter, or I have obtained the written permission of the original data submitter to cite that study.

2. That for each study cited in support of registration or reregistration under FIFRA that is NOT an exclusive use study, I am the original data submitter, or I have obtained the written permission of the original data submitter, or I have notified in writing the company(ies) that submitted data I have cited and have offered to: (a) Pay compensation for those data in accordance with sections 3(c)(1)(F) and 3(c)(2)(D) of FIFRA; and (b) Commence negotiation to determine which data are subject to the compensation requirement of FIFRA and the amount of compensation due, if any. The companies I have notified are. (check one)

[ ] The companies who have submitted the studies listed on the back of this form or attached sheets, or indicated on the attached "Requirements Status and Registrants' Response Form,"

3. That I have previously complied with section 3(c)(1)(F) of FIFRA for the studies I have cited in support of registration or reregistration under FIFRA.

Signature	Date

Name and Title (Please Type or Print)

GENERAL OFFER TO PAY: I hereby offer and agree to pay compensation to other persons, with regard to the registration or reregistration of my products, to the extent required by FIFRA section 3(c)(1)(F) and 3(c)(2)(D).

Signature	Date

Name and Title (Please Type or Print)

EPA Form 8570-31 (4-96)