UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: July 27, 2005

ACTION MEMORANDUM

SUBJECT: Inert Reassessment – 1,1-Difluoroethane (CAS Reg. No. 75-37-6)

FROM: Dan Rosenblatt, Chief
Minor Use, Inerts, and Emergency Response Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

Action: Reassessment of two inert exemptions from the requirement of a tolerance. The two current exemptions are to be maintained.

Chemical: 1,1-Difluoroethane
CFR: 40 CFR part 180.910 [formerly 40 CFR 180.1001(c)] and 40 CFR part 180.930 [formerly 40 CFR 180.1001 (e)]
CAS #: 75-37-6

Use Summary: 1,1-Difluoroethane is employed for aerosol pesticide formulations used for insect control in food and feed-handing establishments and animals. The predominant use of this chemical is in consumer products, including used as an aerosol propellant in food and non-food commodities, as refrigerant, and in the synthesis of 1-chloro-1,1-difluoroethane.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the two exemptions from the requirement of a tolerance for the inert ingredient, 1,1-Difluoroethane, CAS # 75-37-6. I consider the two exemptions established in 40 CFR part 180.910 [formerly 40 CFR180.1001(c)] and in 40

CFR part 180.930 [formerly 40 CFR 40 CFR180.1001(e)] to be reassessed for purposes of FFDCA's section 408(q) as of the date of my signature, below. A Federal Register Notice regarding these tolerance exemptions reassessment decision will be published in the near future.

Lois A. Rossi, Director
Registration Division

Date: 7/27/05

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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MEMORANDUM

SUBJECT: Reassessment of the Two Exemptions from the Requirement of a Tolerance for 1,1-Difluoroethane

FROM: Bipin Gandhi
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

THRU: Pauline Wagner, Inerts Coordinator
Registration Division (7505C)

TO: Dan Rosenblatt, Chief
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

Background

Attached is the science assessment for 1,1-difluoroethane. The purpose of this document is to reassess two existing exemptions from the requirement of a tolerance for residues of this inert ingredient as required under the Food Quality Protection Act (FQPA section 408). This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, environmental fate, ecotoxicity, and exposure profiles of 1,1-difluoroethane. In performing this assessment, the Agency has relied extensively upon reviews of 1,1-difluoroethane previously performed for the Integrated Risk Assessment System (IRIS) and by the High Production Volume Chemical Challenge Program (HPV).

Executive Summary

This report evaluates 1,1-difluoroethane (CAS Reg. No. 75-37-6), a pesticide inert ingredient for which an exemption from the requirement of a tolerance exists for its residues when used as propellant in pesticide formulations applied to raw agricultural commodities under 40 CFR §180.910 and as propellant in pesticide formulations applied to animals under 40 CFR §180.930.

This hazard assessment relies upon assessments of 1,1-difluoroethane performed by IRIS and HPV programs.

Taking into consideration all available information on 1,1-difluoroethane, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to 1,1-difluoroethane when considering inhalation exposure through food commodities and all other nonoccupational sources of inhalation exposure for which there is reliable information. Therefore, it is recommended that the exemptions from the requirement of a tolerance established for residues of 1,1-difluoroethane when used as propellant in pesticide formulations applied to raw agricultural commodities and used as propellant in pesticide formulations applied on animals can be considered reassessed as safe under section 408(q) of the FFDCA.

I. Introduction

This report evaluates 1,1-difluoroethane (CAS Reg. No. 75-37-6), a pesticide inert ingredient for which an exemption from the requirement of a tolerance exists for its residues when used as propellant in pesticide formulations applied to raw agricultural commodities under 40 CFR §180.910 and as propellant in pesticide formulations applied to animals under 40 CFR §180.930. The exemption from tolerances were established on July 29, 1996 (61 FR 39351, FRL 5386-8)

1, 1-Difluoroethane is widely used worldwide as an aerosol propellant in food and non-food commodities, as refrigerant and as an intermediate in the synthesis of 1-chloro-1,1-difluoroethane (refrigerant 142b).

The concentration of 1,1-difluoroethane as a propellant in pesticide formulations ranges from 14% to 78% by weight in the pesticide formulation.

Other names for 1,1-Difluoroethane include: Difluoroethane; ethane, 1,1-difluoro-; ethylene fluoride; ethylidene difluoride; ethylidene fluoride; Freon 152a; Algofrene type 67; HFC 152a; R 152a; Genetron 100; Genetron 152a; Refrigerant 152a (Toxnet SIS, 2005).

II Use Information

Pesticides

The two tolerance exemptions for 1,1-difluoroethane being reassessed in this document are given in Table 1 below.

Table 1. Tolerance Exemptions Being Reassessed in this Document

Tolerance Exemption Expression	40 CFR §	Use Pattern (Pesticidal)	CAS Reg No.	List Classification
1, 1-Difluoroethane (CAS Reg No. 75-37-6)	180.910[1/]	For aerosol pesticide formulations used for insect control in food and feed-handing establishments and animals.	75-37-6	2
1, 1-Difluoroethane (CAS Reg No. 75-37-6)	180.930[2/]	For aerosol pesticide formulations used for insect control in food and feed-handing establishments and animals.		

1. Residues listed in 40 CFR §180.910 [formerly 40 CFR§ 180.1001(c)] are exempted from the requirement of a tolerance when used as inert ingredients in pesticide formulations when applied to raw agricultural commodities.
2. Residues listed in 40 CFR §180.930 [formerly 40 CFR§ 180.1001(e)] are exempted from the requirement of a tolerance when used as inert ingredients in pesticide formulations when applied to animals.

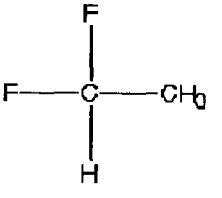
Other Uses

1,1-Difluoroethane is also used as an aerosol in non-food commodities, refrigerant and in the synthesis of 1-chloro-1,1-difluoroethane.

III. Physical and Chemical Properties

Some of the physical and chemical characteristics of 1, 1-difluoroethane are given in Table 2 below.

Table 2. Physical and Chemical Properties for 1, 1-Difluoroethane

Parameters	Value	Source
Structure	 1, 1-difluoroethane	Toxnet SIS, 2005

Molecular Formula	$C_2H_4F_2$	Toxnet SIS, 2005
Molecular Weight	66.1	Toxnet SIS, 2005
Color/form	Colorless, odorless gas	Toxnet SIS, 2005
Melting point	-117°C	Toxnet SIS, 2005
Boiling Point	-24.7°C	Toxnet SIS, 2005
Critical Temperature and pressure	113.3°C @ $4.52x10^6$ Pa	Toxnet SIS, 2005
Solubility	17.8 g/L water @ 25°C	Toxnet SIS, 2005
Density/Specific gravity	0.91 @ 21°C	Toxnet SIS, 2005
Heat of combustion	-4.42 kcal/g	Toxnet SIS, 2005
Heat of vaporization	0.078 kcal/g	Toxnet SIS, 2005
Octanol/Water partition. Coefficient.	Log K_{ow} = 0.75	Toxnet SIS, 2005
Vapor Density	203 (air = 1)	Toxnet SIS, 2005
Vapor Pressure	4,550 mm Hg @ 25°C	Toxnet SIS, 2005

IV. Hazard Assessment

A. Hazard Profile

This hazard assessment relies upon reviewed assessments of 1,1-difluoroethane performed by IRIS and HPV submission to the Agency. The HPV program determined that the submitted data were adequate for the purposes of the HPV challenge program, although some of the robust summaries needed to be enhanced. For the purposes of the tolerance reassessment, the enhanced robust summaries were used.

The IRIS evaluation of 1,1-difluoroehthane states that "1,1-difluoroetathane is a gas mainly used as propellant, refrigerant and as an intermediate in the synthesis of 1-chloro-1,1-difluoriethane. It is non-toxic to rats and mice via inhalation exposure, the main route of exposure. It is non-teratogenic and no adverse effects on reproductive cycles of laboratory animals.

B. Toxicological Data

Acute toxicity:

One acute oral toxicity study for 1,1-difluoroethane was cited in the HPV data. The data were deemed to be of low reliability because of the uncertainties associated with using a gas in

an oral dosing suspension. However, the study reported the approximated lethal dose to be > 1500mg/kg.

No data on dermal toxicity, dermal or eye irritation or dermal sensitization were identified.

1,1-Difluoroethane is practically non-toxic following acute inhalation exposure. Groups of 6 male ChR-CD rats were exposed whole body to concentrations of 0, 66,400, 175,200, 319,000, 383,000 and 437,000 ppm 1,1-difluoroethane for 4 hours. There was one death at the 383,000 ppm concentration and two deaths at 437,000 ppm concentration. During the exposure period, labored breathing, lethargy, and unresponsiveness to sound were observed. Following exposure no clinical signs were observed, and there was no pathology seen at necropsy after the 14-day observation period. . (Haskell Report No 699-75 cited in HPV Robust summaries for 1,1-difluoroethane).

In another study no adverse effect was reported at 200,000 ppm for 2 hours of exposure to male albino rats. (IRIS)

Cardiac/Pulmonary Sensitization:

The effects of 1,1-difluoroethane were studied on the ventricular function of dogs and mice. Concentration of 10 and 20% of 1,1-difluoroethane caused depression of myocardial contractility in dogs.(Aviado and Belje, 1974) In an additional study, male Beagle dogs (12/group) were exposed to 50,000 or 150,000ppm for 5 minutes. The dogs were given a control injection of epinephrine (0.008mg/kg) iv prior to exposure and a challenge injection of the same dose was given to the animals after a 5 minute exposure to 1,1-difluoroethane. Cardiac arrhythmia was observed in 3 dogs at the 150,000 ppm exposed group, but no response was seen at 50,000 ppm .(HPV Robust Summaries) In another study, the bronchopulmonary system of mice was influenced by 1 to 2% concentration of 1,1-difluoroethane and respiration by 2.5 to 5% of 1,1-difluoroethane. The chemical did not cause spontaneous cardiac arrhythmia in the mouse, but it did cause sensitization of the heart of epinephrine in mice that had experimental bronchopulmonary lesions (Brody, Watanabe and Aviado, 1974).

Subchronic toxicity:

Subchronic studies did not report any adverse effects from inhalation exposure to 1,1-difluoroethane.

When CD male rats were exposed to 100,000 ppm for 6/hours/day for 5/days per week for 2 weeks no adverse effects were observed. Reversible depression of central nervous system was seen during exposure, but resolved when exposure ceased. (IRIS). Similar results were

observed when the above sub-chronic study was repeated (Haskell study No. 699-75 cited in IRIS).

Chronic Toxicity/Carcinogenicity

In a two year chronic study male and female Crl:CDBR rats were exposed whole body to 0, 2000, 10,000 and 25,000 ppm 1,1-difluoroethane for 6/hrs day 5/days/wk. At the end of the study there was a dose-related increase in urinary fluoride concentration and excretion in males and females at the two higher doses and serum creatinine was significantly elevated at these two higher doses. There was no increase in mortality in the treated groups or any treatment related pathology. There was no carcinogenicity at any dose level (Haskell study No. 8-82 cited in HPV Robust Summary for 1,1-difluoroethane).

In another study no chronic adverse effects were observed except mild chronic irritation when make rats were exposed to 100,000 ppm for 16 hours/day for 2 months (IRIS).

Genetic Toxicity:

Reliable genotoxicity studies generally showed negative results. The *in vitro* chromosome aberration test in human lymphocytes was weakly positive.

Du Pont studied the 1,1-difluoroethane for bacterial reverse mutation with and without activation and the results were negative (Haskell Report No. 4032 cited in HPV Robust Summary for 1,1-difluoroethane).

In vitro chromosome aberration test in human lymphocytes showed statistically significant increases in the proportion of the aberrant cells both with and without activation. The study authors concluded that 1,1-difluoroethane gave a weakly positive response. (Haskell Report No. 4032 cited in HPV Robust Summary for 1,1-difluoroethane).

An *in vivo* rat Micronucleus Test in Sprague Dawley rats dosed with 1,1-difluoroethane did not show any evidence of chromosome damage or bone marrow cell toxicity when administered by whole body inhalation. (DuPont Study No. 5426 cited in HPV Robust Summary for 1,1-difluoroethane).

Development Toxicity:

Pregnant female rats were exposed to 0, 5000 and 50,000 ppm of 1,1-difluoroethane 6 hours per day from gestation day 6 to 15. No clinical signs of maternal toxicity or body weight changes were reported. No gross pathological abnormalities were observed in ovaries, uterine horns, vital organs or tissues of the treated animals. The number of corpora lutea, implantation sites, and live fetuses per litter were similar in all groups. Fetal body measurements in treated groups did not differ from controls. There were no statistical significant soft tissue abnormalities. The NOAEL for maternal toxicity and for development toxicity was 50,000 ppm and LOAEL was not determined in ether case (Haskell Report No. 437-79 cited in HPV Robust Summaries for 1,1-difluoroethane).

Reproductive Toxicity:

The two-year rat whole body inhalation study for 1,1-difluoroethane in conducted by Haskell Laboratory (Report No. 8-82 in HPV Robust Summary for 1,1-difluoroethane, EPA, 2001), included data on the histopathology and weights of the reproductive organs of the treated animals. No histopathological or weight effects were reported for any dose group of either sex in the study. The Du Pont SHE Excellence Center Robust Summary (HPV Report) considered the reliability of this aspect of the original Haskell Report to be medium, because a suboptimal study design was used.

No standard reproductive toxicity studies for 1,1-difluoroethane were identified.

C. Metabolism And Pharmacokinetics:

No data were identified for the metabolism and pharmacokinetics of 1,1-difluoroethane.

D. Special Considerations for Infants and Children:

Based on the inhalation exposure to the animals and therefore, lack of concern for human health effects, a safety factor analysis has not been used to assess the risks resulting from the use of 1,1-difluoroethane as a pesticide inert ingredients (as propellant) and an additional tenfold safety factor for the protection of infants and children is also not necessary.

V. Exposure Assessment:

Exposure of 1,1-difluoroethane to the general population is solely via inhalation route because of its gaseous characteristics. Humans may get inhalation exposure through the use of food and non-food aerosol containers. Exposure of 1,1-difluoroethane is practically negligible through its use as refrigerant because it is used in sealed systems and a small amount may escape through leaks will be dissipated and diluted in the air. Since 1,1-difluoroethane is non-toxic to rats and mice and it is non-carcinogen, non-teratogen and has no adverse effects on reproductive cycles of laboratory animals, it is not expected to have adverse effects on humans through the exposure of 1,1-difluoroethane.

VI. Aggregate Exposures

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

For 1,1-difluoroethane, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the lack of human health concerns associated with exposure to 1,1-difluoroethane.

VII. Cumulative Exposure

Section 408(b)(2)(D)(v) of the FFDCA 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."

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to 1,1-difluoroethane and any other substances and this material does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that 1,1-difluoroethane has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/

VIII. Environmental Fate Characterization/Drinking Water Considerations

According to model of gas/particle partitioning of semi-volatile organic compounds in the atmosphere , 1,1-difluoroethane is expected to exist solely as a vapor in the ambient atmosphere. The atmospheric half-life of about 472 days at an atmospheric concentration. This long atmosphere lifetime of this chemical suggests some 1,1-difluoroethane is expected to diffuse into the stratosphere above the ozone layer where it will slowly degrade due to direct photolysis from UV-radiation (HPV Robust Summaries for 1,1-fluoroethane).

The estimated half-life for a model river and model lake are 2 and 77 hours respectively. 1,1-Difluoroethane is not expected to adsorb to suspended solids and sediment in water based on

the measured log value of 0.75. 1,1–Difluoroethane is expected to volatilize rapidly from the surfaces (HPV Robust Summaries for 1,1-difluoroethane).

As per EPIWIN Version 3.05, 1,1-difluoroethane is distributed 99.9%, 0.111%, 0.01% and <0.01% in air, water, soil and sediment respectively. Bioconcentration factor of 2 was determined using a measured log K_{ow} of 0.75 which suggest that bioconcentration in aqueous organisms is low (HPV Robust Summaries for 1,1-fluoroethane).

Ecotoxicity:

The 96 hours LC_{50} for fish is calculated at 733/mg/L. The 46 hours EC_{50} for Daphnia is calculated at 720mg/L. The 96 hours EC_{50} for Algae is calculated at 419 mg/L concentration. All three values are theoretical values based on ECOSAR model. Based on the ECOSAR model and high Henry Law Constant 1,1-difluoroethane is unlikely to represent an unacceptable risk to aquatic organisms or wildlife (HPV Robust Summaries for 1,1-difluoroethane).

IX. Human Health Risk Characterization

1,1-Difluoroethane is practically non-toxic following acute or chronic inhalation exposures. It is not a developmental or reproductive toxicant in rat studies and is negative for cancer in a two year rat inhalation study. It is not mutagenic in a *in vitro* bacterial reverse mutation assay and shows some weak clastogenicity in an *in vitro* human lymphocyte chromosome aberration test, but further evaluation of its ability to cause chromosome damage in and *in vivo* micronucleus test was negative. There is evidence that 1,1-difluoroethane can cause cardiac effects is some species, most notably heart arrhythmia in the dog.

Evaluations of IRIS and HPV data have concluded that there are no safety concerns associated with the use of 1,1-fluoroethane as propellant used in pesticide formulations for insect controls in food and feed establishments and as propellant used in pesticide formulations used on animals. Taking into consideration all available information on 1,1-difluoroethane, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to 1,1-difluoroethane when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is concluded that the exemptions from the requirement of a tolerance established for residues of 1,1-difluoroethane in/on raw agricultural commodities and animals can be considered reassessed as safe under section 408(q) of the FFDCA.

X. Ecotoxicity and Ecological Risk Characterization

Based on the information submitted above, 1, 1-difluoroethane binding to sediments or the concentration in water in less than 0.1% which is based on theoretical calculations.

Therefore, no hazard to environment. The concentration of 1,1-difluoroethane will be very low in water and thus no hazard to eco system.

XI **References**

Aviado, D.M. and M.A. Belej. 1975. Toxicity of aerosol propellants in the respiratory and circulatory systems. V. Ventricular function in the dog. Toxicology 3, 79-86.

Brody, R.S., T. Watanabe and D.M. Aviado. 1975. Toxicity of aerosol propellants in the respiratory and circulatory systems. III. Influence of bronchopulmonary lesion on cardiopulmonary toxicity in the mouse. Toxicology 2, 173-184.

EPA. 2001. Du Pont SHE Excellence Center Robust Summary for 1,1-difluoroethane 2001. Posted on the EPA' s HPV Challenge Program ChemRTK Web Site on August 22, 2001 at <http://www.epa.gov/chemrtk/1difluoro/c13124.pdf >.

IRIS. 2005. 1,1-difluoroethane; CASRN 75-37-6. <http://www.epa.gov/iris/subst/0665.htm>.

Toxnet SIS. 2005. Specialized Information Service. On-line Scientific Search Engine, National Library of Medicine, National Institute of Health.< http://toxnet.nlm.nih.gov>. Search term: CAS No: 75-37-6; Hazardous Substance Databank (last revised: *02/14/2003*); accessed *2005.*