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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

DATE: September 28, 2005

ACTION MEMORANDUM

SUBJECT: Inert Reassessment–n-Hexyl Alcohol; CAS# 111-27-3

FROM: Pauline Wagner, Chief Pauline Wagner 9/29/05
Inert Ingredient Assessment Branch
Registration Division (7505C)

TO: Lois A. Rossi, Director Donald R Stubb
Registration Division (7505C)

I. FQPA REASSESSMENT ACTION

Action: Reassessment of two inert exemptions from the requirement of a tolerance. The reassessment decision is to maintain each of the two inert tolerance exemptions "as-is."

Chemical: n-hexyl alcohol

CFR: 40 CFR part 180.910 and 40 CFR part 180.930

CAS Registry Number and Name: 111-27-3; 1-Hexanol (9CI)

Use Summary: Commercially, n-hexyl alcohol is used as a solvent and in the manufacture of perfume, antiseptics, and plasticizers. In addition, it is used as a flavor volatile in food and is approved as a U.S. Food and Drug Administration Direct Food Additive under 21 CFR 172.515. As an inert ingredient in pesticide formulations, n-hexyl alcohol is a solvent or cosolvent in a number of pesticide products, including those used on agricultural food crops, animals, ornamental plants, and in residential-use pesticides such as insect sprays.

List Reclassification Determination: The current List Classification for n-hexyl alcohol is 4B; it will retain its current Classification.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the two exemptions from the requirement of a tolerance for the inert ingredient n-hexyl alcohol (CAS #111-27-3) and with the List reclassification determinations, as described above. I consider the two exemptions established in 40 CFR part 180.910 and 40 CFR part 180.930 to be reassessed for purposes of FFDCA's section 408(q) as of the date of my signature, below. A *Federal Register* Notice regarding this tolerance exemption reassessment decision will be published in the near future.

Lois A. Rossi, Director
Registration Division

Date: 9/30/05

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

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OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

September 28, 2005

MEMORANDUM

SUBJECT: Reassessment of the Two Exemptions from the Requirement of a Tolerance for n-Hexyl Alcohol

FROM: Kathleen Martin, Chemist KathMA. 9/28/05
Inert Ingredient Assessment Branch
Registration Division (7505C)

TO: Pauline Wagner, Chief Pauline Wagner 9/29/05
Inert Ingredient Assessment Branch
Registration Division (7505C)

BACKGROUND

Attached is the science assessment for n-hexyl alcohol. The purpose of this document is to reassess the two existing exemptions from the requirement of tolerance for residues of n-hexyl alcohol as required under the Food Quality Protection Act (FQPA). This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of n-hexyl alcohol.

EXECUTIVE SUMMARY

This report evaluates n-hexyl alcohol, a pesticide inert ingredient for which two exemptions from the requirement of a tolerance exist for its residues under 40 CFR 180.910 and 40 CFR 180.930. Commercially, n-hexyl alcohol is used as a solvent and in the manufacture of perfume, antiseptics, and plasticizers (Elvers et al 1989; Lington and Bevan 1991). In addition, it is used as a flavor volatile in food (IPCS 2001) and is approved as a U.S. Food and Drug Administration (FDA) Direct Food Additive under 21 CFR 172.515. As an inert ingredient in pesticide formulations, n-hexyl alcohol is a solvent or cosolvent in a number of pesticide products, including those used on agricultural food crops, animals, ornamental plants, and in residential-use pesticides such as insect sprays.

Overall, n-hexyl alcohol is of low acute toxicity by the oral and dermal routes (Toxicity Category III); however, it is moderately irritating to the skin and severely irritating to the eye (Lington and Bevan 1991). In repeated oral studies, no significant systemic toxicity was observed. Based on available information, n-hexyl alcohol has not been reported to be neurotoxic or mutagenic and, there is no evidence that n-hexyl alcohol is carcinogenic. Some developmental toxicity was observed (slight increase in resorptions per litter in a developmental toxicity study and testicular atrophy in a 13-week feeding study); however, these effects were noted at very high doses, in fact at doses at the limit dose.

EPA expects that exposure to n-hexyl alcohol is widespread, though not at high concentrations. It is likely that exposures from residues found in food, drinking water, or through residential uses are much lower than the levels where any effects were noted. Linear saturated aliphatic alcohols, which include n-hexyl alcohol, are ubiquitous in nature—they have been detected in almost every known fruit and vegetable (IPCS 1998). In addition to its natural occurrence, FDA permits n-hexyl alcohol to be deliberately added to foods as a flavoring substance and adjuvant. JECFA has evaluated the use of n-hexyl alcohol as a flavoring agent. They reported that there is no "safety concern at current levels of intake when used as a flavouring agent" (IPCS 2001). n-Hexyl alcohol is readily biodegradable so it is unlikely that residues would be found on foods harvested and consumed or in drinking water. For residential uses, EPA does not expect significant exposure via the dermal route as n-hexyl alcohol is not readily taken up by the skin (Lington and Bevan 1991). Inhalation exposure modeling shows that the level of n-hexyl alcohol expected in the air would be low.

Thus, taking into consideration all available information on n-hexyl alcohol, EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to n-hexyl alcohol used as an inert ingredient when considering dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the two exemptions from the requirement of a tolerance established for residues of n-hexyl alcohol can be considered reassessed as safe under section 408(q) of FFDCA.

I. Introduction

This report evaluates n-hexyl alcohol, a pesticide inert ingredient for which two exemptions from the requirement of a tolerance exist for its residues when used in used in accordance with good agricultural practice as an inert ingredient in pesticide formulations applied to growing crops or to raw agricultural commodities (RACs) after harvest (40 CFR 180.910) and to animals (40 CFR 180.930).

EPA expects that exposure to n-hexyl alcohol is widespread, though not at high concentrations. n-Hexyl alcohol occurs naturally in most fruits and vegetables (IPCS 1998). Commercially, n-hexyl alcohol is used as a solvent and in the manufacture of perfume, antiseptics, and plasticizers (Elvers et al 1989; Lington and Bevan 1991). In addition, it is used as a flavor volatile in food (IPCS 2001) and is approved as a U.S. Food and Drug Administration (FDA) Direct Food Additive under 21 CFR 172.515.

II. Use Information

A. Pesticides

n-Hexyl alcohol is used as an inert ingredient only; there are currently no registered pesticide products containing n-hexyl alcohol as an active ingredient. As an inert ingredient, n-hexyl alcohol is a solvent or cosolvent in a number of pesticide products, including those used on agricultural food crops, animals, ornamental plants, and in residential-use pesticides such as insect sprays. The exemptions from the requirement of a tolerance for n-hexyl alcohol are provided in Table 1 below.

Table 1. Exemptions from the Requirement of a Tolerance

Tolerance Exemption Expression	CAS Registry Number/Name	40 CFR 180	Use Pattern (Pesticidal)
n-Hexyl alcohol	111-27-3 1-Hexanol (9CI)	.910[a]	solvent, cosolvent
n-Hexyl alcohol		.930[b]	solvent, cosolvent

[a]Residues listed in 40 CFR 180.910 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to RACs after harvest.

[b]Residues listed in 40 CFR 180.930 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals.

B. Other Uses

n-Hexyl alcohol is used as a solvent, as a basic material in the perfume industry, in the manufacture of antiseptics, and in the production of plasticizers (Elvers et al 1989; Lington and Bevan 1991). In addition to its industrial uses, n-hexyl alcohol is added to foods and beverages as a flavor volatile (IPCS 2001); there is one FDA Direct Food Additive for n-hexyl alcohol (see Table 2).

Table 2. FDA Direct Food Additive Uses for n-Hexyl Alcohol

Name	21 CFR 172	Use Pattern
Hexyl alcohol	.515	Synthetic flavoring substances and adjuvants used in food in the minimum quantity required to produce their intended effect, and otherwise in accordance with all the principles of good manufacturing practice.

III. Physical and Chemical Properties

Some of the physical and chemical characteristics of n-hexyl alcohol, along with its structure and nomenclature, are found in Table 3.

Table 3. Physical and Chemical Properties of n-Hexyl Alcohol

Parameter	Value	Reference
Structure		
CAS #	111-27-3	
Empirical Formula	$C_6H_{14}O$	
Molecular Weight	102.17	Merck 2005
Common Names	amylcarbinol, pentylcarbinol, 1-hydroxyhexane, 1-hexanol	Merck 2005
Physical State	liquid	Merck 2005
Melting Point	-51.6°C	Merck 2005
Boiling Point	157°C	Merck 2005
Water Solubility	slightly soluble	Merck 2005
Other Solubility	miscible with alcohol, ether	Merck 2005
Relative Density (water=1)	0.8153@ 25°C	Merck 2005
Vapor Pressure	0.124 kPa @ 25°C [0.93 mm Hg]	NIOSH 2002
log Kow	2.03	NIOSH 2002
Henry's Law Constant	$1.71\times^{-5}$ atm-m^3/mole	U.S. EPA 2004a

IV. Hazard Assessment

A. Hazard Profile

A number of sources were considered in assessing the hazard for the use of n-hexyl alcohol as an inert ingredient in pesticide formulations. Data that were relied upon are discussed below in their relevant sections. n-Hexyl alcohol has been identified as a chemical meeting the criteria of EPA's High Production Volume (HPV) Challenge Program[1]. In 2001 its sponsor, ExxonMobil Chemical Company (2001), submitted a test plan. To the extent possible, the test plan data were considered in this risk assessment.

B. Toxicological Data

Overall, n-hexyl alcohol is of low acute toxicity by the oral and dermal routes (Toxicity Category III from 40 CFR 156.62); however it is moderately irritating to the skin and severely irritating to the eye (Lington and Bevan 1991). In repeated oral studies, no significant systemic toxicity was observed. Based on available information, n-hexyl alcohol has not been reported to be neurotoxic or mutagenic and, there is no evidence that n-hexyl alcohol is carcinogenic. Some developmental toxicity was observed (slight increase in resorptions per litter in a developmental toxicity study and testicular atrophy in a 13-week feeding study); however, these effects were noted at very high doses.

Acute Toxicity

A summary of the acute toxicity data along with the 40 CFR 156.62 Acute Toxicity Categories is provided in Table 4. Lington and Bevan (1991) noted that n-hexyl alcohol is moderately irritating to the eye of rabbits and severely irritating to the skin of rabbits; no details were provided regarding parameters such as the reversibility of the irritation.

[1]HPV chemicals are those that are manufactured or imported into the United States in volumes greater than one million pounds per year. There are approximately 3,000 HPV chemicals that are produced or imported into the United States. The HPV Challenge Program is a voluntary partnership among industry, environmental groups, and EPA which invites chemical manufacturers and importers to provide basic hazard data on the HPV chemicals they produce/import. The goal of this program is to facilitate the public's right-to-know about the potential hazards of chemicals found in their environment, their homes, their workplace, and in consumer products.

Table 4. Summary of Acute Toxicity Data for n-Hexyl Alcohol

Parameter		Toxicity Value *40 CFR 156.62 Category*	Reference
Oral LD_{50}	rat	4,590 to 4,870 mg/kg *Toxicity Category III*	Lington and Bevan 1991
	mouse	4,000 mg/kg *Toxicity Category III*	Lington and Bevan 1991
Dermal LD_{50}, rabbit		2,530 mg/kg *Toxicity Category III*	Lington and Bevan 1991
Inhalation LC, rat		>1,000 mg/kg @ >8 hours	Sax 1987
Eye Irritation, rabbit		moderately irritating	Lington and Bevan 1991
Skin Irritation, rabbit		severely irritating	Lington and Bevan 1991

Subchronic Toxicity

In 1998 the the Joint World Health Organization (WHO)/Food and Agriculture Organization (FAO) Expert Committee on Food Additives (JEFCA) evaluated 38 flavoring flavoring agents, one of which was n-hexyl alcohol. The Committee's report (IPCS 1998) summarized two subchronic toxicity studies, as follows; no further details were provided:

> "Two groups of male and female rats were fed hexyl alcohol at dietary levels of 0.25 and 0.50% for 13 weeks; a third group was fed 1% (reported to be equivalent to 577 mg/kg bw per day) for weeks 1-10, then 2, 4 and 6% for weeks 11, 12 and 13, respectively. Food consumption was decreased in the high-dose females, but no significant haematological changes, differences in urine analyses or histopathological effects were observed...."

> "In a 13-week study, hexyl alcohol at levels of 0.5 and 1% in the diet, or at a dose level of 1000 mg/kg bw per day in gelatin capsules, was given to dogs. At a dose of 1000 mg/kg bw per day, 4 out of 5 dogs died. Haematology, serum chemistry and urine analyses revealed no differences in treated dogs relative to controls. There was gastrointestinal inflammation in the mid- and high-dose groups. Congestion of the viscera and testicular atrophy were observed at the high dose. A NOAEL of 1%, which corresponds to a daily intake of 230-695 mg/kg bw, was determined from this study...."

Neurotoxicity

In an experiment to investigate peripheral neuropathies, Perbellini et al (1978) administered n-hexyl alcohol to 20 rats by intraperitioneal[2] injection (i.p.) daily, six days/week for 30 weeks. n-Hexyl alcohol was dissolved in peanut oil and administered in a single daily dose of 102.5 mg/kg/day. After 30 weeks of treatment, the investigators observed no clinical signs of peripheral neuropathy: neither muscle weakness, ataxia, loss of equilibrium, nor abnormal movements were seen. The following were noted on neurophysiological examinations: Motor conduction velocity in treated rats was not statistically different from that of control rats. The sensory conduction velocity in treated rats was decreased significantly. The distal motor latency, which the investigators considered to be the most indicative electromyographic change in toxic polyneuropathies, was not altered in the treated rats nor was the sensory potential amplitude. On the morphological examination of nerve fibers of animals treated with n-hexyl alcohol, no clear abnormalities were found. The average body weight of the control rats was greater than that of the treated rats; however, the differences were not statistically-significant.

The research concluded that n-hexyl alcohol produced equivocal signs of neurotoxicity in the peripheral nervous system. EPA believes that effects similar to these observed via the i.p. route would not be seen if the animals were exposed through the dermal or inhalation route. When an animal is dosed via the dermal or inhalation route, biotransformation by the gastrointestinal cells, liver or lung occurs (Casarett and Doull 1986). The phenomenon of removing chemicals after oral absorption before entering the general systemic circulation is referred to as first-pass effect (Casarett and Doull 1986). Materials entering the organism via the i.p. route may not be transformed in the same manner.

Mutagenicity

The European Commission's International Uniform Chemical Information Database[3] (IUCLID) reports the results of two *in vitro* mutagenicity tests which use the *Salmonella typhimurium* reverse mutation assay. The first experiment used n-hexyl alcohol concentrations of 8; 40; 200; 1,000; or 5,000 μg/plate and the second experiment used concentrations of 6.25; 25; 100; 400; or 1,600 μg/plate. Both experiments were done with and without activation. All results were negative. (European Commission 2000)

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[2]Note: EPA's Office of Pesticide Programs does not normally report data collected by the i.p. route; however, these were the only data available for neurotoxicity.

[3]IUCLID is a database of existing chemicals that is being compiled by the European Chemicals Bureau (ECB). IUCLID is the basic tool for data collection and evaluation within the EU-Risk Assessment Programme; it has been accepted by the OECD as the data exchange tool under the OECD Existing Chemicals Programme.

Carcinogenicity

Patty's Industrial Hygiene And Toxicology (Lington and Bevan 1991) describes a study to test the tumor-promoting activity of n-hexyl alcohol on mouse skin after an initiating dose of 7, 12-dimethylbenz(*a*)anthracene. A volume of 20 μL of the test material dissolved in cyclohexane (20 g n-hexyl alcohol in 100 mL of cyclohexane) was applied to treated mouse skin three times a week for 60 weeks. No tumors were observed.

Developmental and Reproductive Toxicity

To examine the validity of Richardson's Law[4], Nelson (Nelson et al 1990) reported a summary of his findings from a series of studies investigating the developmental toxicology of aliphatic alcohols administered by inhalation to rats. For n-hexyl alcohol, Nelson (Nelson et al 1990; Lington and Bevan 1991) exposed 15 pregnant rats via inhalation to the maximally attainable vapor concentration of n-hexyl alcohol (3,500 mg/m^3 or 840 ppm) for 7 hours/day on gestation days (GD) 1 to 19. For developmental toxicology evaluations, dams were sacrificed on GD 20. Fetuses were removed, weighed, sexed, and examined for external malformations.

The only sign of developmental toxicity observed was a slight increase in resorptions/litter; no maternal toxicity was observed. The developmental NOAEL was not determined; the developmental LOAEL is 3,500 mg/m^3, based on increased resorptions. The maternal NOAEL is 3500 mg/m^3; the maternal LOAEL was not determined.

	Developmental Toxicity	**Maternal Toxicity**
NOAEL (mg/m^3)	not determined	3,500
LOAEL (mg/m^3)	3,500	not determined

C. Metabolism and Pharmacokinetics

Patty's Industrial Hygiene And Toxicology (Lington and Bevan 1991) reports that n-hexyl alcohol is not readily taken up by the skin. Metabolic studies in rabbits show that oxidation to hexanoic acid is the major pathway, mediated by alcohol dehydrogenase and aldehyde dehydrogenase. Direct conjugation with glucuronic acid is a minor pathway. (Lington and Bevan 1991)

[4]In the late 1800's Richardson observed that, among the alcohols, toxicity to adult animals generally increased with chain length, up to about six carbons, after which the toxicity decreased.

D. Special Considerations for Infants and Children

n-Hexyl alcohol is of low acute toxicity by the oral and dermal routes (Toxicity Category III). Nelson (Nelson et al 1990) noted that the only sign of developmental toxicity was an increase in resorptions/litter at a very high dose (3,500 mg/m^3 or 840 ppm); no maternal toxicity was observed. IPCS (1998) reports the results of a 13-week oral study in dogs where the animals were fed n-hexyl alcohol in their diet. At the high dose (1000 mg/kg bw per day) testicular atrophy was noted. EPA expects that any exposure to n-hexyl alcohol used as an inert ingredient in pesticide formulations would occur at a level much lower than those noted in these two studies. Based on the available information, a safety factor analysis has not been used to assess the risks resulting from the use of n-hexyl alcohol; therefore, an additional tenfold safety factor for the protection of infants and children is unnecessary.

V. Environmental Fate Characterization and Drinking Water Considerations

The Office of Pesticide Programs Environmental Fate and Effects Division (EFED) has reviewed (U.S. EPA 2002, U.S. EPA 2005b) the fate and environmental effects of the aliphatic alcohols by reviewing the available data and considering Structure Activity Relationships (SAR). As a group, the C6 through C8 alcohols, which includes n-hexyl alcohol, are water soluble and mobile in terrestrial and aquatic environments, moving mainly with the water phase to surface and ground water receptors. Volatility from soil (vapor pressure 0.93 mm Hg), and water (Henry's law constant of $1.71\times^{-5}$ atm m^3/mole) and microbially-mediated degradation are expected to limit transport to surface and ground water from applications or releases to land, with biodegradation being the major route of environmental dissipation. Fugacity modeling predicts that portioning of n-hexyl alcohol will be 31% mass amount in water and 66% mass amount in soil. Predicted dissipation half-lives range from 1.0 to 1.5 days in rivers and 15 to 20 days in lakes. These data suggest that n-hexyl alcohol is not persistent in the environment.

n-Hexyl alcohol may contaminate shallow aquifer groundwater; however, biologically-mediated degradation in both aerobic and anaerobic conditions will limit loadings, thus concentrations. Based on the high volatility of most aliphatic alcohols and aeration sequences used in many drinking water utilities, it is unlikely that most of these compounds will be found in treated water at concentrations equivalent to those in the environment. Available ambient water monitoring data indicate that many short chain aliphatic alcohols are found in surface water in the low- to mid-ppb range. There are no ambient water quality criteria or drinking water maximum contaminant or health advisory levels for any of the aliphatic alcohols. (U.S. EPA 2002)

VI. Exposure Assessment

Individuals may be exposed to n-hexyl alcohol through the oral, dermal, and inhalation routes of exposure. In terms of a pesticide inert ingredient, EPA expects that exposure to n-hexyl alcohol would primarily be through the oral route, via consumption of agricultural crops to which this inert ingredient has been applied as a solvent or cosolvent, and exposure through drinking water. Additional dermal and inhalation exposure may occur from residential use of pesticide products containing n-hexyl alcohol on ornamental plants and lawns, as well as from the use of antifouling paints, and indoor and outdoor pest sprays. Expected food, drinking water, and residential exposures are discussed below.

Food and Drinking Water

As an inert ingredient of pesticide products applied to growing crops, RACs after harvest, or to animals, potential human exposure would be via the oral route, through consumption of food to which a n-hexyl alcohol-containing pesticide product has been applied, or through drinking water. Because of its environmental fate properties, EPA expects that drinking water exposures would be low as n-hexyl alcohol readily biodegrades in soil and water.

n-Hexyl alcohol is expected to be found in food, but at low levels. Linear saturated aliphatic alcohols, which include n-hexyl alcohol, are ubiquitous in nature—they have been detected in almost every known fruit and vegetable (IPCS 1998); some examples are provided in Table 5. In addition to its natural occurrence, FDA permits n-hexyl alcohol to be added to food "in the minimum quantity required to produce their intended effect." And, JECFA has evaluated the use of n-hexyl alcohol as a flavoring agent (IPCS 2001).

Table 5. n-Hexyl Alcohol Found in Foods

Food	Exposure	Reference
Kiwi Fruit	detected in volatile component	as reported in NIH 2005
Farine (processed cassava product)	detected in volatile component	as reported in NIH 2005
Beaufort cheese	detected in volatile component	as reported in NIH 2005
Bacon flavor	detected in volatile component	as reported in NIH 2005
Roasted filberts	detected in volatile component	as reported in NIH 2005
Chickpeas	detected in volatile component	as reported in NIH 2005
Raw beef	detected in volatile component	as reported in NIH 2005
Clams	detected in volatile component	as reported in NIH 2005
Dried legumes	0.07 ppm in volatile component	as reported in NIH 2005
Nectarines	0.2 ppm in volatile component	as reported in NIH 2005
Garlic bulb	0.2 ppm in volatile component	as reported in NIH 2005
Gelatins & puddings	0.3 ppm	as reported in NIH 2005
Non-alcoholic beverages	6.6 ppm	as reported in NIH 2005
Baked goods	18 ppm	as reported in NIH 2005
Candy	21 ppm	as reported in NIH 2005
Ice cream	26 ppm	as reported in NIH 2005

Residential

Exposure to n-hexyl alcohol's use as an inert ingredient may occur in residential settings through its use on ornamentals such as nursery plants (trees, flowers, shrubs, ground cover, house plants), grasses (including golf courses, turf, and sod), ant mounds, indoor and outdoor pest sprays (including those used on pets, crack and crevice, home perimeters, institutions such as schools), wood preservatives, and home vegetable gardens.

Residential exposure may occur through the inhalation or dermal route. To estimate worst-case residential indoor inhalation exposure, EPA modeled a scenario where an aerosol paint product contained 95% n-hexyl alcohol and was sprayed for 20 minutes in an enclosed utility room (i.e., "Indoor Aerosol Paint"). To estimate worst-case dermal exposure, EPA modeled a scenario where indoor-use of latex paint contained 95% n-hexyl alcohol (i.e., "Latex Paint" scenario). Using E-FAST[5] (U.S. EPA 2004b) and standard model assumptions (model results are provided in Appendix A), EPA determined that the Average Daily Concentration (which is an exposure metric for inhalation exposure) for n-hexyl alcohol would be 2.0 mg/m^3 (8.4 ppm); for dermal exposure, the Average Daily Dose (which is an exposure metric for dermal exposure) is 0.11 mg/kg/day. Provided in Table 6 is a summary of the E-Fast results. Note that for outdoor-use products, EPA believes that exposure would be no greater than for indoor use.

Table 6. Modeled Exposure Estimates for Inhalation and Dermal Exposure to n-Hexyl Alcohol

Exposure Route	E-FAST Scenario Used to Model Exposure	Percent n-Hexyl Alcohol	Exposure[a]
Inhalation	Indoor Aerosol Paint	95	2.0 mg/m^3 (8.4 ppm)
Dermal	Latex Paint[b]	95	0.11 mg/kg/day

[a]For inhalation exposure, Average Daily Concentration (mg/m^3 and ppm); for dermal exposure, Average Daily Dose (mg/kg/day).

[b]The "Latex Paint" model run also provides an estimate for inhalation exposure; however, this assessment relies on the inhalation estimate obtained from the "Indoor Aerosol Paint" scenario because it yields a higher, more conservative estimate.

[5]The E-FAST model is used by EPA's Office of Pollution, Prevention and Toxics to conduct New Chemicals exposure assessment. It was developed to provide screening-level estimates of the concentrations of chemicals released from consumer products. Modeled estimates of concentrations and doses are designed to reasonably overestimate exposures, for use in screening level assessment.

These estimates are considered worst-case for several reasons:

(1) In the E-FAST run, a high concentration of n-hexyl alcohol was assumed (i.e., 95%), it is unlikely that all indoor residential-use products containing n-hexyl alcohol as an inert ingredient contain it at such a concentration. For example, a cursory review of several Material Safety Data Sheets (MSDS) for residential-use pesticides containing n-hexyl alcohol as an inert ingredient shows n-hexyl alcohol concentrations ranging from 0.1 to 40 percent.

(2) E-FAST is designed as a screening tool, modeled estimates of concentrations and doses are designed to reasonably overestimate exposures; and

(3) The E-FAST scenarios that would yield the greatest exposures (indoor aerosol paint for inhalation and latex paint for dermal) were used.

Therefore, EPA does not expect actual exposure from residential use of n-hexyl alcohol as an inert ingredient to exceed these modeling estimates.

VII. Aggregate Exposures

In examining aggregate exposure, the Federal Food, Drug, and Cosmetic Act (FFDCA) section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other nonoccupational 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 n-hexyl alcohol, 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 n-hexyl alcohol as an inert ingredient in pesticide formulations.

VIII. Cumulative Exposure

Section 408(b)(2)(D)(v) of 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 n-hexyl alcohol and any other substances and, n-hexyl alcohol 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 n-hexyl alcohol 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's Office of Pesticide Programs 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/.

IX. Human Health Risk Characterization

Taking into consideration all available information on n-hexyl alcohol, EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to n-hexyl alcohol used as an inert ingredient when considering dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Overall exposure due to the inert use of n-hexyl alcohol is expected to result in human exposure below any dose level that would produce any adverse effect. Therefore, it is recommended that the two exemptions from the requirement of a tolerance established for residues of n-hexyl alcohol can be considered reassessed as safe under section 408(q) of FFDCA.

Overall, n-hexyl alcohol is of low acute toxicity by the oral and dermal routes (Toxicity Category III); however it is moderately irritating to the skin and severely irritating to the eye (Lington and Bevan 1991). In repeated oral studies, no significant systemic toxicity was observed. Based on available information, n-hexyl alcohol has not been reported to be neurotoxic or mutagenic and, there is no evidence that n-hexyl alcohol is carcinogenic. Some developmental toxicity was observed (slight increase in resorptions per litter in a developmental toxicity study and testicular atrophy in a 13-week feeding study); however, these effects were noted at very high doses, in fact at doses at the limit dose. EPA expects that any exposure to n-hexyl alcohol used as an inert ingredient in pesticide formulations would occur at a level much lower than the levels where any effects were noted.

Linear saturated aliphatic alcohols, which include n-hexyl alcohol, are ubiquitous in nature—they have been detected in almost every known fruit and vegetable (IPCS 1998). In addition to its natural occurrence, FDA permits n-hexyl alcohol to be deliberately added to foods as a flavoring substance and adjuvant. Specific limits are not stipulated, though the regulation permitting this use (40 CFR 172.515) does say that synthetic flavoring substances and adjuvants "used in food in the minimum quantity required to produce their intended effect...." JECFA has evaluated the use of n-hexyl alcohol as a flavoring agent. They reported that there is no "safety concern at current levels of intake when used as a flavouring agent" (IPCS 2001). n-Hexyl alcohol is readily biodegradable so it is unlikely that residues would be found on foods harvested and consumed or in drinking water.

For residential uses, EPA does not expect significant exposure via the dermal route as n-hexyl alcohol is not readily taken up by the skin (Lington and Bevan 1991). Worst-case chronic inhalation exposure is estimated to be 8.4 ppm or 2.0 mg/m^3. In a study conducted by the inhalation route (Nelson et al 1990; developmental toxicity) effects were only seen at a 840 ppm or 3,500 mg/m^3, which is a very high dose. Thus, the Agency believes that residential exposure resulting from the inert use of n-hexyl alcohol will not be of concern.

X. Ecotoxicity and Ecological Risk Characterization

EFED finds that based on their ecotoxicity estimates, n-hexyl alcohol is practically nontoxic on an acute basis. For freshwater and marine/estuarine fish, and *Daphnia magna* acute toxicity estimates range from 5 to greater than 100 mg/L. For mysid shrimp, acute estimates range from 3 and 36 mg/L; and for green algae, 12 to 73 mg/L. Chronic toxicity for fish is estimated to be from 2 to 14 mg/L. Terrestrial animal toxicity based on available rat data indicate that n-hexyl alcohol is practically nontoxic on an acute basis.

Based on acute toxicity values from tests with similar alcohols, n-hexyl alcohol is expected to be no more than moderately toxic to fish and aquatic invertebrates on an acute basis. Tests with freshwater and marine/estuarine fish and aquatic invertebrates provided a range of acute toxicity endpoints from 3 mg/L (moderately toxic) to greater than 100 mg/L (practically non-toxic). Toxicity to green algae was in the low to moderate range; acute endpoints ranged from 12 to 73 mg/L. Chronic toxicity testing with fish showed effects at concentrations in the 2 to 14 mg/L range. Based on available data from acute testing with rats, n-hexyl alcohol is practically nontoxic to mammals on an acute basis. (U.S. EPA 2002; U.S. EPA 2005a)

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