

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



OFFICE OF PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

June 11, 2009

**MEMORANDUM**

SUBJECT: Inert Ingredient Tolerance Reassessment for Pigment Red 48 – Erratum

FROM: Kerry Leifer, Team Leader  
Inert Ingredient Assessment Branch  
Registration Division (7505P)

A handwritten signature in black ink, appearing to read "Kerry Leifer", written over the printed name in the "FROM:" field.

TO: PV Shah, Chief  
Inert Ingredient Assessment Branch  
Registration Division (7505P)

On February 10, 2006, a tolerance reassessment document for the inert ingredient Pigment Red 48 was completed. That document stated that the tolerance exemption under 40 CFR 180.920 for Pigment Red 48 was reassessed "as is." While the 40 CFR 180.920 tolerance exemption expression for Pigment Red 48 does not include a CAS Reg. No., the reassessment document associated the CAS Reg. No. of 3564-21-4, which is C.I. Pigment Red 48, disodium salt (also known as 2-naphthalenecarboxylic acid, 4-[2-(5-chloro-4-methyl-2-sulfophenyl)diazenyl]-3-hydroxy-, sodium salt (1:2)).

Based on additional information related to the use of the term "Pigment Red 48" and the commercial usage of Pigment Red 48 as a pigment, it has been determined that it is the calcium salt form of C.I. Pigment Red 48 (also known as C.I. Pigment Red 48:2) that is the substance that has usage as a pigment rather than C.I. Pigment Red 48, disodium salt. C.I. Pigment Red 48, calcium salt (1:1) has a CAS Reg. No. of 7023-61-2 and a CA Index Name of 2-naphthalene-carboxylic acid, 4-[(5-chloro-4-methyl-2-sulfophenyl)azo]-3-hydroxy-, disodium salt.

Therefore, a correction to the February 10, 2006, tolerance reassessment document is made to include CAS Reg. No. 7023-61-2 under the tolerance exemption expression of Pigment Red 48 under 40 CFR 180.920.



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DATE: February 10, 2006

**ACTION MEMORANDUM**

**SUBJECT:** Inert Reassessment Pigment Red 48, CAS Reg. No. 3564-21-4

**FROM:** Pauline Wagner, Chief *Pauline Wagner 2/10/06*  
Inert Ingredient Assessment Branch  
Registration Division (7505C)

**TO:** Lois A. Rossi, Director  
Registration Division (7505C)

**I. FQPA REASSESSMENT ACTION**

**Action:** Reassessment of one inert exemption() from the requirement of a tolerance. THE EXEMPTION IS BEING REASSESSED AS-IS.

**Chemical:** Pigment Red 48

**CFR:** 40 CFR part 180.920

**CAS Registry Number and Name:** CAS Reg. No. 3564-21-4, Pigment Red 48

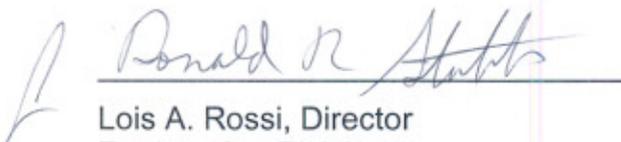
**Use Summary:** The only pesticide use of Pigment Red 48 is used as a dye for coloring the seeds before planting. The predominant use of this chemical is in consumer products, including, paints, ink, solvents, plastics and rubber.

**List Reclassification Determination:** There is no reclassification and it retains the original classification of 40 CFR 180.920

*The current List Classification for Pigment Red 48 is 3. Because EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to Pigment Red 48 used as inert ingredient in pesticide formulations, the List Classification for Pigment Red 48 will change from List 3 to List 4B.*

## II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the one exemption from the requirement of a tolerance for the inert ingredient Pigment Red 48, CAS Reg. No. 3564-21-4. with the List reclassification determination, as described above. I consider the one exemption established in 40 CFR part 180.9 20 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

2/17/06  
Date:

cc: Debbie Edwards, SRRD  
Joe Nevola, SRRD

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WASHINGTON, D.C. 20460



OFFICE OF PREVENTION,  
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SUBSTANCES

February XXX, 2006

**MEMORANDUM**

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance for Pigment Red 48 (CAS Reg. No. 3564-21-4)

FROM: Bipin Gandhi   
Inert Ingredient Assessment Branch (IIAB)  
Registration Division (7505C)

TO: Pauline Wagner, Chief  
Inert Ingredient Assessment Branch (IIAB)  
Registration Division (7505C)

**Background**

Attached is the science assessment for Pigment Red 48. Pigment Red 48 has one exemption from the requirement of a tolerance under 40 CFR 180.920 as a dye for seed treatment use only as listed in Table 1. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of Pigment Red 48. The purpose of this document is to reassess the existing exemption from the requirement of a tolerance for residues of Pigment Red 48 when used as an inert ingredient in pesticide formulations as required under the Food Quality Protection Act (FQPA).

**Executive Summary**

This report evaluates Pigment Red 48, a pesticide inert ingredient for which an exemption from the requirement of a tolerance exists for its residues when used as a dye for seed treatment only in pesticide formulations applied to growing crops only under 40 CFR 180.920.

Pigment Red 48 is a synthetic dye. It is an azo derivative from naphthalene so it falls under the category of naphthalene moiety dyes. Pigment Red has many salts. They are for example, mono and disodium, calcium, barium, strontium and manganese salts. The salts of Pigment Red 48 are used in commerce and not the basic Pigment Red 48. Therefore, the exemption from the requirement of a tolerance under 40 CFR 180.920 is limited to Pigment Red 48 as the disodium salt.

A structure activity relationship analysis for Pigment Red 48 was conducted by the Office of Pollution Prevention and Toxics (OPPT) Structure Activity Team (SAT). The OPPT assessment concluded that Pigment Red 48 is not likely absorbed from the skin or the GI tract as the intact

material. It has good absorption from the lung; however, this is not expected to be the route of exposure from its use as a seed treatment dye. The azo chemical bond will be reduced in the intestines with good absorption of the reduction products. Red Dye 48 has a low octanol-water coefficient ( $K_{ow}$ ) of -1.25, thus is not likely to bioaccumulate in the environment. Red Dye 48 is soluble, non volatile, and likely to be mobile. Leaching to ground water is expected because of its low estimated soil partition coefficient. Potential to volatilize from surface waters is very low and atmospheric degradation is expected to be fairly rapid.

No significant health concerns were identified, and so Pigment Red 48 was given a low concern for human health effects. There is low concern for toxicity to aquatic organisms. It is classified as not readily biodegradable. There is little or no probability of exposure to Pigment Red 48 expected from its use as an inert ingredient in pesticide formulations, and therefore, risk concerns are not expected by the Agency.

Taking into consideration all available information on Pigment Red 48, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to Pigment Red 48 when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the exemption from the requirement of a tolerance established for residues of Pigment Red 48 when used as a dye for seed treatment only can be considered reassessed as safe under section 408(q) of the FFDCA.

## **I. Introduction**

This report provides a qualitative assessment for Pigment Red 48, a pesticide inert ingredient used as a dye for seed treatment. This chemical has an exemption from the requirement of a tolerance under 40 CFR 180.920.

Pigment Red 48 is a synthetic dye. It is an azo derivative from naphthalene so it falls under the category of naphthalene moiety dyes. Pigment Red has many salts. They are for example, mono and disodium, calcium, barium, strontium and manganese salts. The salts of Pigment Red 48 are used in commerce and not the basic Pigment Red 48. Therefore, the exemption from the requirement of a tolerance under 40 CFR 180.920 is limited to Pigment Red 48 as the disodium salt.

## **II. Use Information**

### **A. Pesticide Uses**

Pigment Red 48 is exempted from the tolerance requirement of a tolerance when used in formulations as a dye for seed treatment only (40 CFR 180.920) as shown table 1 below.

**Table 1. Pesticide Uses**

CFR Citation
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40 CFR §	Inert Ingredients	Limits	Uses	
180.920*	Pigment Red 48	For seed treatment use only	Dye	3564-21-4/ Pigment Red 48 (as disodium salt)

\*Residues listed in 40 CFR 180.920 are exempt 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 only.

### B. Other Uses

The other uses of Pigment Red 48 (in salt form) include uses in paint, ink, solvents, plastics, and rubber.

### III. Physical and Chemical Properties

Table 2. Physical and Chemical Properties<sup>1</sup>

Pigment Red 48 CAS Reg. NO. 3564-21-4	
Parameter	Value
Structure	
Chemical Name	2-Naphthalenecarboxylic acid, 4-(5-chloro-4-methyl-2-sulfohenyl)azo]-3-hydroxy-, disodium salt (9 CI)
Molecular formula	C <sub>18</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>6</sub> SN <sub>2</sub>
Physical Form/color	Red powder
Odor	Odorless
Molecular Wt.	464.79° C (estimated)
Melting Point	350° C (estimated)
Boiling Point	. 810° C (estimated)
Vapor Pressure	8.62e 0.22 mm Hg (estimated)
Henry's Law Constant	1.46e 0.18 atm-m <sup>3</sup> /mole
Log K <sub>ow</sub>	-1.25 (estimated)
Log K <sub>oc</sub>	2.80 (estimated)
Log BCF	0.5 (estimated)

<sup>1</sup> EPIWIN

#### **IV. Hazard Assessment**

Pigment Red 48 is not expected to pose a hazard when used as a dye for seed treatment pesticide formulations. The amount used as a dye is very small, 1% or less in formulation. The available data indicate that Pigment Red 48 is not toxic to animals.

##### **A. Hazard Profile**

The information for this profile was derived from studies identified in searches of BIBRA International Limited (1990). In addition, a structure activity relationship analysis of Pigment Red 48 was conducted by the Office of Pollution Prevention and Toxics (OPPT) Structure Activity Team. The OPPT assessment concluded Pigment Red 48 is of low concern for human health, with no significant health concerns identified.

##### **B. Toxicological Data**

###### **Acute Toxicity:**

The oral LD50 for the rat is greater than 2 g/kg bw. No additional information is available (Cowley, 1985; FSTP, 1968; Gosselin et al. 1976; NPIRI, 1983 all as cited in BIBRA, 1997).

###### **Skin Irritation:**

A 5% solution of Pigment Red 48, the disodium salt, cause no irritation when in covered contact with the skin of six rabbits for 24 hours (Pennisi and Casper, 1992 as cited in BIBRA, 1997).

###### **Chronic Toxicity:**

No relevant data identified.

###### **Reproductive/Developmental Toxicity:**

No relevant data identified.

###### **Carcinogenicity:**

No relevant data identified.

###### **Genotoxicity:**

Pigment Red 48 showed no evidence of mutagenic activity in Ames bacterial tests with *Salmonella typhimurium*. It was tested in presence and absence of a liver metabolic activation system (Loser, 1988; Milvy & Kay, 1978; NPIRI, 1983 as citer in BIBRA (1997)). However, the study protocol may be inadequate because only 1 ug/plate was tested compared to current standard of testing at up to 5 mg/plate.

### **C. Special Consideration for Infants and Children**

Pigment Red 48 has a high LD<sub>50</sub> value for rats (2g/kg), which is the only toxicity data available for review. There are no data currently available for chronic and subchronic toxicities. In addition, no developmental or reproductive and carcinogenicity studies were identified. However, Pigment Red is not mutagenic. This chemical is used and approved only as a dye for seed treatment use only in pesticide formulations. The amount applied to seeds is small compared to the weight of the seeds. By the time seeds germinate most of the dye will be adsorbed by the soil and eventually degraded with little of the dye available for potential plant uptake.

In the worst-case scenario, residues from the use of the dye are expected to be in micrograms per kilogram of plant grown from the treated seed. The amount of dye will be further reduced in the grown crop since the edible portion of the crop is small compared to the whole plant. When the hay from the plant grown from the seed treated with Pigment Red 48 is fed to the animals, the residue of the dye in meats and meat products is expected to be several orders of magnitude less than levels in the animal, therefore, far below levels of concern. Based on the available exposure and toxicity information, safe history of similar uses, a safety factor analysis has not been used to assess the risks resulting from the inert pesticidal use of Pigment Red 48, and therefore, an additional tenfold safety factor for the protection of infants and children is unnecessary.

### **V. Environmental Fate Characterization/Drinking Water Considerations**

The environmental fate of Pigment Red 48 [C.I. Pigment Dye 48, Disodium salt (1:1)], here forth referred to as Red Dye 48 may result in its likelihood of reaching surface and ground water and will limit its likelihood of bioaccumulating in the environment. There were no measured physical-chemical properties or environmental transformation and/or occurrence data located in the readily available open literature. Therefore, this assessment is based solely on estimated properties. Red Dye 48 is not expected to rapidly biodegrade in the environment, primary degradation is likely to occur on the order of weeks and ultimate degradation (mineralization) on the order of months. The compound is classified as not readily biodegradable. Red Dye 48 has a low octanol-water coefficient ( $K_{ow}$ ) of -1.25, thus is not likely to bioaccumulate in the environment. Red Dye 48 is soluble, non volatile, and likely to be mobile. Leaching to ground water is expected because of its low estimated soil partition coefficient. Potential to volatilize from surface waters is very low and atmospheric degradation is expected to be fairly rapid.

OPPT and OPP modeled estimates for environmental fate indicates that drinking water exposures may occur but concentrations are likely to be low in community system because clarity is a primary treatment goal. Migration to ground water drinking water sources is likely due to its estimated partition coefficient of approximately 600.

### **VI. Exposure Assessment**

The only pesticide inert ingredient use of Pigment Red 48 is as a dye for seed treatment. The amount used for seed treatment is very low compared to the weight of seeds. In addition, the chemical will degrade in the soil and any amount of plant uptake from the germination of seeds

treated with Pigment Red 48 expected to be negligible. In addition, any amount that is taken up by the plant will also be subject to degradation or metabolism. Therefore, exposure to this chemical from the treated crops grown from treated seeds is expected to be negligible. There will be no residential exposure since there are no residential uses.

## **VII. Aggregate Exposure**

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 garden, lawns, or buildings (residential and other indoor uses). As stated above under 'Exposure Assessment' there will not be any measurable exposure through food, water or residential uses.

For Pigment Red 48, 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 the exposure to Pigment Red 48 when used in pesticide formulations as a dye for seed treatment only.

## **VIII. 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 or toxicity, EPA has not made a common mechanism of toxicity safety finding as to pigment Red 48, and any other substances, and Pigment Red 48 do not appear to produce toxic metabolites produced by other substances. For the purpose of its tolerance action, therefore, EPA has not assumed that Pigment Red 48 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**

Based upon the OPPT Structure Activity Team's structure activity relationship analysis, Pigment Red 48 is of low concern for human health effects. Pigment Red 48 is not expected to be absorbed by the skin with poor or no absorption occurring via the GI tract. Absorption of Pigment Red 48 in lungs is expected to be moderate to good for lower molecular weight species, but no identifiable toxicological endpoints are associated with inhalation exposure to Pigment Red 48.

Taking into consideration all available information on Pigment Red 48, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to Pigment Red 48 when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the exemption from the requirement of a tolerance established for residues of Pigment Red 48 when used as an inert ingredient in pesticide formulations can be considered reassessed as safe under section 408(q) of the FFDCFA.

**X. Ecotoxicity and Ecological Risk Characterization**

Pigment Red 48 may be considered moderately to slight toxic to most aquatic organisms based on an SAR analog using anionic dyes with 2 acid groups. The lowest estimated effects concentration was associated with indirect chronic effects to algae (greater than 2.0 ppm) due to shading from the dye. Chronic effects to daphnia were estimated to be greater than 5.0 ppm and fish chronic effects were greater than 3.0 ppm. All acute effects were at higher concentrations and ranged from greater than 16 ppm for algae to greater than 50 ppm for daphnia. There were no effects data located in the Agency's Ecotox Database (<http://www.epa.gov/ecotox>).

Pigment Red 48 is not expected to bioaccumulate in the environment. Therefore, based on potential exposures and estimated toxicity to aquatic and terrestrial organisms (using available rat, mouse, and rabbit data as surrogate for all terrestrial animals), ecological concerns for listed and non-listed species are not likely from the use of Pigment Red 48 as an inert ingredient in pesticide products unless application rates exceed 25 pounds per acre per application based on an acute effect to listed species and 40 pounds per acre on a yearly basis based on chronic effects. Applications rates which are far exceed those expected from its use in pesticide products as a dye for seed treatment only.

**Table 3. Ecosar predicted data\***

Organism	End Pt	Predicted mg/L (ppm)
Fish	Chronic Value	> 3.0
Fish	LC50	> 5.0
Daphnid	LC50	> 54.0
Green Algae	EC50	> 16.0
Daphnid	Chv	> 5.0
Green Algae	Chv	> 2.0

\* ECOSAR Run

**XI. References:**

BIBRA. 1997. British Industrial Biological Research Association (BIBRA)--Toxicity Profile: Pigment Red 48, 48:1, 48:2, 48:3, 48.4. Woodmansterne Rd., Carshalton, Surrey, UK, 4 pp.

CFR 40. Code of Federal Regulations. 40. Part 180.920 Exemptions from the requirement of a tolerance.

Environmental Protection Agency (2005). Structure Activity Team Report (# 205-15) from Office of Pollution Prevention and Toxics. March 15, 2005.