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

OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES

# ACTION MEMORANDUM

**SUBJECT:** Inert Reassessment – Propyl Gallate (CAS Reg. No. 121-79-9)

**FROM:** Pauline Wagner, Chief
Inert Ingredient Assessment Branch

**TO:** Lois A. Rossi, Director
Registration Division

## I. FQPA REASSESSMENT ACTION

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

**Chemical:** Propyl Gallate

| CFR Citation | | | | CAS Reg. No. /Name |
|---|---|---|---|---|
| 40 CFR § | Inert Ingredients | Limits | Uses | |
| 180.910* | Propyl gallate | (none) | Antioxidant | 121-79-9<br>Benzoic acid, 3,4,5-trihydroxy-, propyl ester |
| 180.930** | Propyl gallate | (none) | Antioxidant | 121-79-9<br>Benzoic acid, 3,4,5-trihydroxy-, propyl ester |

*Residues listed in 40 CFR 180.910 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 or to raw agricultural commodities after harvest.
**Residues listed in 40 CFR 180.930 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 animals.

**Use Summary:** Propyl gallate is used as an antioxidant in pesticide formulations with typical concentrations 0.25% in formulation. It is also used as an antioxidant in consumer food and cosmetic products.

**List Reclassification Determination:** The current List Classification for propyl gallate 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 propyl gallate when used

as an antioxidant in pesticide formulations, the List Classification for propyl gallate will change from List 3 to List 4B.

## II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the two exemptions from the requirement of a tolerance for the inert ingredient propyl gallate, CAS Reg. No. 121-79-9 and with the List reclassification determination, as described above. I consider the two exemptions established in 40 CFR part 180.910 [formerly 40 CFR 180.1001(c)], and 180.930 [formerly 40 CFR 180.1001 (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 this tolerance exemption reassessment decision will be published in the near future.

Lois A. Rossi

Lois A. Rossi, Director
Registration Division

Date: 12/30/05

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC
SUBSTANCES

December 29, 2005

**MEMORANDUM**

SUBJECT: Reassessment of Two Exemptions from the Requirement of a Tolerance For Propyl Gallate (CAS Reg. No. 121-79-9)

FROM: Keri Grinstead
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505C)

TO: Pauline Wagner, Chief 12/30/05
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505C)

## Background

Attached is the science assessment for propyl gallate. Propyl gallate has two exemptions from the requirement of a tolerance; one under 40 CFR 180.910 when applied to growing crops and raw agricultural commodities after harvest, and one under 40 CFR 180.930 when applied to animals, 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 propyl gallate. The purpose of this document is to reassess the existing exemptions from the requirement of a tolerance for residues of propyl gallate when used as an inert ingredient in pesticide formulations as required under the Food Quality Protection Act (FQPA).

## Executive Summary

This report evaluates the existing exemptions from the requirement of a tolerance for propyl gallate (CAS Reg. No. 121-79-9) when used as an inert ingredient in pesticide formulations under 40 CFR 180.910, when applied to growing crops or raw agricultural commodities after harvest, and under 40 CFR 180.930, when applied to animals.

Propyl gallate is used as an antioxidant in pesticide formulations with typical concentrations $\leq 0.25\%$ in formulation. It is also used as an antioxidant in consumer food and cosmetic products. It currently has an ADI of 0-1.4 mg/kg bw/day established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

Propyl gallate, administered orally to rats and rabbits, was quickly metabolized and excreted. It has low acute oral toxicity, and is only slightly irritating to the skin and

eyes of rabbits. In sensitization testing on guinea pigs, it was considered nonsensitizing at challenge concentrations $\leq 0.1\%$, with sensitization reactions only seen after long induction periods and at challenge concentrations $\geq 0.5\%$. No effects from chronic oral exposure to propyl gallate occurred at levels up to 1% (1.5 g/kg/day). Propyl gallate was noncarcinogenic in dietary studies using rats and mice and in a dermal study using guinea pigs. It was also considered nonmutagenic in all but one of many mutagenesis tests (with and without activation). Fetal effects were observed from a repeated oral dosage of 2000 mg/kg bw/day (rat), a dosage that was maternally toxic. Other developmental studies indicated no fetal abnormalities at dosages $\leq$ 880 mg/kg bw/day (rat), 300 mg/kg bw/day (mice), and 250 mg/kg bw/day (hamsters).

The environmental fate of propyl gallate will limit its likelihood of reaching either surface (drinking water) or ground water or bioaccumulating in the environment. Propyl gallate is expected to biodegrade in the environment with ultimate aerobic degradation estimated to be weeks and primary degradation in days. Migration to ground water drinking water sources is possible, but will be limited by its primary degradation and its moderate adsorption to soils and sediments; therefore concern for exposures via drinking water is likely to be low.

The primary route of exposure to propyl gallate from its use as an antioxidant in pesticide formulations is expected to be through consumption of food to which this chemical has been applied. Additional exposure may occur via the dermal route from residential use of pesticide products containing this chemical; however, inhalation exposure is not expected based on its nonvolatile nature.

Propyl gallate is considered to be moderately toxic to aquatic organisms. Ecological concerns for listed and nonlisted species are not likely from the use of propyl gallate as an inert ingredient in pesticide products.

Taking into consideration all available information on propyl gallate, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to propyl gallate when used as an antioxidant in pesticide formulations 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 propyl gallate, as listed in Table 1, can be considered reassessed as safe under section 408(q) of the FFDCA.

## I. Introduction

This report provides a qualitative assessment for propyl gallate, an inert ingredient used as an antioxidant in pesticide formulations. Propyl gallate has two exemptions from the requirement of a tolerance, one under 40 CFR 180.910 when applied to growing crops and raw agricultural commodities after harvest and one under 40 CFR 180.930 when applied to animals.

Antioxidants react quickly with free radicals, terminating chain reactions and slowing oxidation of substrates. This process ultimately slows oxidation of industrial materials during prolonged storage and substantially increases food shelf life by delaying the deterioration of food odors and flavors.

## II. Use Information

### A. Pesticide Uses

Propyl gallate is used as an antioxidant in pesticide formulations. Typical concentrations of propyl gallate in pesticide products range between 0.01 and 0.25%. The exemptions from the requirement of a tolerance for residues of propyl gallate when used as an inert ingredient in pesticide formulations are provided in Table 1 below.

**Table 1. Pesticide Uses**

| CFR Citation | | | | CAS Reg. No. /Name |
|---|---|---|---|---|
| 40 CFR § | Inert Ingredients | Limits | Uses | |
| 180.910* | Propyl gallate | (none) | Antioxidant | 121-79-9<br>Benzoic acid, 3,4,5-trihydroxy-, propyl ester |
| 180.930** | Propyl gallate | (none) | Antioxidant | 121-79-9<br>Benzoic acid, 3,4,5-trihydroxy-, propyl ester |

*Residues listed in 40 CFR 180.910 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 or to raw agricultural commodities after harvest.

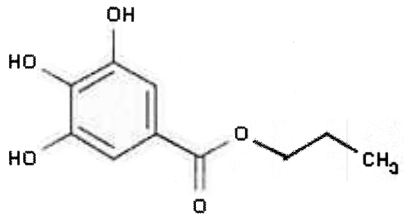
**Residues listed in 40 CFR 180.930 are exempt from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals.

### B. Other Uses

According to Abdo et al. (1986), propyl gallate is "used as an antioxidant to stabilize fats, oils, and fat-containing foods against peroxidation and rancidity and to stabilize vitamins, essential oils and perfumes in cosmetics. Cosmetic preparations may contain as much as 5% propyl gallate, but most often concentrations are less than 0.1%. Amounts in foods (such as fats, oils, baked goods, candy, dairy products and beverages) are less than 0.02%". A list of FDA approved uses is included in Appendix A.

## Physical and Chemical Properties

**Table 2. Physical and Chemical Properties**

| | Propyl Gallate (CAS Reg. No. 121-79-9) | |
|---|---|---|
| Parameter | Value | Source |
| Structure |  | ChemID[1] |
| Molecular formula | $C_{10}H_{12}O_5$ | ChemID |
| Molecular Wt. | 212.20 | ChemID |
| Melting Point | 130° C<br>Experimental | ChemID |
| Water solubility | 3500 mg/L (25° C)<br>Experimental | ChemID |
| Henry's Law Constant | 6.30E-12 atm-$m^3$/mole(25° C)<br>Estimated | ChemID |
| log P (Octanol-water) | 1.8<br>Experimental | ChemID |

[1]ChemIDplus Advanced on TOXNET (http://www.toxnet.nlm.nih.gov/index.html)

## Hazard Assessment

### A. Hazard Profile

This hazard assessment was developed primarily using the 1989 Toxicity Profile of Propyl Gallate from BIBRA Information Services, Ltd., the 1985 Cosmetic Ingredient Review (CIR) Final Report on the Safety Assessment of Propyl Gallate, a National Toxicology Program (NTP) Technical Report Series No. 240 Carcinogenesis Bioassay of Propyl Gallate, reports from the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA), as well as selected journal articles.

## B. Metabolism and Pharmacokinetics

Propyl gallate was quickly metabolized and excreted when administered orally to rats and rabbits. CIR (1985) reported that "When fed to rats, most of the Propyl Gallate was passed in the feces as the original ester. The urinary components detected were the original ester and gallic acid, and these were excreted completely within 24 hours". When administered orally to rabbits, 79 percent of the administered dose of propyl gallate was excreted in the urine, "72 percent as 4-methoxygallic acid glucuronide" and "6.7 percent as unconjugated phenolic compounds. Minor metabolites included pyrogallol (free and conjugated) and free 4-methoxy gallic acid" (CIR 1985).

## C. Toxicological Data

### Acute Oral

Based on the oral $LD_{50}$ values, propyl gallate is of low acute oral toxicity when administered to animals.

| Species | Oral $LD_{50}$ | Reference |
|---|---|---|
| Rat | 2.1 – 3.8 g/kg bw | CIR 1985 |
| Mouse | 1.7 – 3.5 g/kg bw | BIBRA 1989 |
| Hamster | 2.48 g/kg bw | BIBRA 1989 |
| Rabbit | 2.75 g/kg bw | BIBRA 1989 |
| Pig | > 2 – 6 g/kg bw | BIBRA 1989 |

### Dermal Irritation

According to the CIR (1985) propyl gallate was not considered a primary irritant to the skin of rabbits and guinea pigs.

| Species | Dose/Vehicle/Test | Result | Reference |
|---|---|---|---|
| Guinea pig | 10% in propylene glycol applied to shaved skin for 48 hours | No local lesions or primary irritation | CIR 1985 |
| Rabbit | <1 percent in a lipstick Primary skin irritation test - applied to intact and abraded skin, three 24-hour applications | Not a primary irritant | |
| Rabbit | 0.003 percent in suntan cream Primary skin irritation – intact and abraded, three 24-hour applications | No edema, not a primary skin irritant | |

| Species | Dose/Vehicle/Test | Result | Reference |
|---|---|---|---|
| Rabbit | 0.003 percent in suntan oil Primary skin irritation – intact, three 6-hour applications | Practically nonirritating | CIR 1985 |

**Acute Eye Irritation**

The only eye irritation data available are from studies which used cosmetic formulations containing <1 percent propyl gallate. These products were considered nonirritating when tested on the eyes of rabbits.

| Species | Product | Result | Reference |
|---|---|---|---|
| Rabbit | Lipstick containing <7% propyl gallate | Nonirritant | CIR 1985 |
| Rabbit | Sun protection stick containing 0.003% propyl gallate | Nonirritant | |
| Rabbit | Suntan cream containing 0.003% propyl gallate | Nonirritant | |
| 6 Rabbits for each formulation | 6 cosmetic formulations each containing 0.003% propyl gallate | Nonirritant | |

**Dermal Sensitization (CIR 1985)**

As summarized in the 1985 CIR report, three separate studies using guinea pigs considered propyl gallate less sensitizing and requiring a much longer induction period via the cutaneous route, yielding sensitization reactions only at challenge doses ≥ 0.5%. It was considered nonsensitizing at 0.1%.

**Subchronic Oral Toxicity**

Rats and pigs were fed diets containing 0.035 – 0.50% or 0.2% propyl gallate for 3 months. There were no effects on growth, reproduction, organ weights, blood chemistry values, morphology of blood cells, or histopathological changes of tissues of the treated animals at any of the tested concentrations (CIR 1985).

According to the 1989 BIBRA Toxicity Profile, "Dietary levels of 5% over 14 days were lethal to mice. A reduced growth rate was the only overt toxic effect reported when the dose was lowered to 2.5%. A comprehensive microscopic examination of the tissues at post-mortem revealed no adverse effects in mice (10/sex/group) given 0.08, 0.15, 0.3, 0.6, or 1.2% in the diet for 13 wk.

Likewise there was no evidence of toxicity, apart from a slight growth depression when the treatment schedule for the two higher dose levels was extended to 2 years using 100 mice, equally divided by sex, per group."

**Chronic Oral Toxicity**

According to the 1985 CIR report, of rats fed diets containing 0 to 5% propyl gallate for two years, patchy hyperplasia of the stomach was observed at the 5% dosage. No significant toxic effects were observed in three groups of mice fed diets containing 0, 0.5, or 1.0% (1.5 g/kg/day) propyl gallate for 90 weeks.

**Mutagenicity**

The 1985 CIR report summarize the results of mutagenicity testing of propyl gallate as follows:

"Results of Ames tests, chromosomal aberration assays, cytogenetic assays, dominant lethal assays, and host-mediated assays indicated that Propyl Gallate was nonmutagenic both with and without metabolic activation, except for one chromosomal aberration assay. Propyl Gallate enhanced the mutagenic activity of N-hydroxy-2-acetylaminofluorine and 4-nitroquinolone-1-oxide in an Ames test using *S. typhimurium* strains TA98 and TA100, respectively. Metabolic activation was required for this to occur."

**Carcinogenicity**

Chronic toxicity and carcinogenicity studies of propyl gallate were conducted on rats and mice, each maintained on diets containing 0, 0.6, or 1.2% propyl gallate for 103 weeks. Under the conditions of the studies, propyl gallate was not considered to be carcinogenic (Abdo, K. M., et al. 1986) and (NTP 1982).

Propyl gallate (20%) in lanolin was applied to the ears of six male guinea pigs five days per week for 6 weeks. While disruption of normal cellular organization was evident during treatment, it was determined not to be an early stage in the development of skin cancer. No skin tumors were detected two years after treatment (BIBRA 1985).

**Developmental/Reproductive Toxicity**

The following are summaries from the 1989 BIBRA document:

"Slight retardation in foetal development was observed in rats given 2000 mg/kg bw/day in the diet throughout pregnancy, a dosing schedule which also caused a marked suppression of maternal body weight gain and food consumption."

There was no evidence of teratogenicity or embryotoxicity in a study of pregnant rats given 350 or 880 mg/kg bw/day. Of those females allowed to deliver normally, the appearance, behavior, and organ weights of their offspring were normal. Rats receiving dosages of up to 300 mg/kg bw/day on days 6-15 of pregnancy were similarly unaffected.

No abnormalities or effects on fetal survival or body weight were seen after administration of up to 300 mg/kg bw/day to mice on days 6-15 of pregnancy and up to 250 mg/kg bw/day to hamsters on days 6-10 of pregnancy.

"There was no increase in foetal abnormalities or evidence of embryotoxicity in rabbits (10-13/group) given daily doses of up to 250 mg/kg bw by stomach tube on days 6-18 of pregnancy."

According to the summary in the 1985 CIR report, female rats fed 0.5 g of propyl gallate had substantially increased rates of fetal resorptions. "However, in four separate teratogenesis studies, Propyl Gallate at doses up to 2.01 g/kg was nonteratogenic in rats, rabbits, mice, or hamsters."

### D. Special Consideration for Infants and Children

Fetal effects were only seen at a dosage level that was also maternally toxic (2000 mg/kg bw/day). Other studies indicated no fetal abnormalities at dosages $\leq$ 880 mg/kg bw/day (rat). The dose level where fetal effects were observed is likely orders of magnitude greater than the expected exposures from the inert ingredient use of propyl gallate in pesticide products. Based on this information, there is no concern, at this time, for increased sensitivity to infants and children to propyl gallate from its use as an inert ingredient (antioxidant) in pesticide products. For these same reasons, a safety factor analysis has not been used to assess risk and, therefore, the additional tenfold safety factor for the protection of infants and children is also unnecessary.

## V. Environmental Fate Characterization/Drinking Water Considerations

The environmental fate of propyl gallate will limit its likelihood of reaching either surface (drinking water) or ground water or bioaccumulating in the environment. Propyl gallate is expected to biodegrade in the environment with ultimate aerobic degradation estimated to be weeks and primary degradation in days. Propyl gallate is soluble, nonvolatile, and moderately mobile. Leaching to ground water is likely in sandy or porous soils, however, mitigated in other soils due to biodegradation. While atmospheric degradation is expected to be rapid, the potential to volatilize from surface waters is very low.

OPP-modeled estimates for environmental fate indicate concern for exposures to propyl gallate via drinking water is likely to be low. This conclusion is based on its rapid

primary degradation (estimated to be in days) and soil adsorption which will increase removal during flocculation, coagulation and sedimentation. Migration to ground water drinking water sources is possible, but will be limited by it primary degradation and its moderate adsorption to soils and sediments (Koc approximately 1200).

## VI. Exposure Assessment

For the general population, the majority of exposure to propyl gallate comes from its use in consumer food and cosmetic products. Propyl gallate is used as an antioxidant in consumer food and cosmetic products. It is affirmed as GRAS (Generally Recognized As Safe) by the FDA (Food and Drug Administration) and has a current ADI (Acceptable Daily Intake) of 0-1.4 mg/kg bw/day, as established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

Propyl gallate is approved for use as an antioxidant in pesticide formulations applied to growing crops and raw agricultural commodities after harvest and to animals. The primary route of exposure from its use as an antioxidant in pesticide formulations is expected to be through consumption of food to which this chemical has been applied. Migration to ground water drinking water sources is possible, but will be limited by its primary degradation and its moderate adsorption to soils and sediments; therefore, concern for exposures via drinking water is likely to be low. Dermal exposure from residential use of pesticide products containing propyl gallate is possible; however, inhalation exposure is not expected based on its nonvolatile nature.

## 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 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 propyl gallate, 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 propyl gallate when used as an antioxidant in pesticide formulations.

## 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 propyl gallate and any other substances, and propyl gallate does not appear to produce toxic metabolites produced by other substances. For the purpose of these tolerance actions, therefore, EPA has not assumed that propyl gallate 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

Propyl gallate is approved for use as an antioxidant in pesticide formulations applied to growing crops and raw agricultural commodities after harvest and to animals. Propyl gallate is quickly metabolized and excreted by the body, has low acute oral toxicity, and is only slightly irritating to the skin and eyes of rabbits. In guinea pig testing, it was considered nonsensitizing at challenge concentrations $\leq 0.1\%$, with sensitization reactions only observed after long induction periods and at challenge concentrations $\geq 0.5\%$. No effects from chronic oral exposure occurred at dietary levels up to 1% (1.5 g/kg/day). Propyl gallate was determined to be noncarcinogenic in oral and dermal animal studies and nonmutagenic in Ames tests, in all but one chromosomal aberration assay, and in cytogenetic and dominant lethal assays. Fetal effects were seen at an oral dosage level of 2000 mg/kg bw/day, a dosage that was maternally toxic. Other studies indicated no fetal abnormalities at dosages $\leq$ 880 mg/kg bw/day (rat), 300 mg/kg bw/day (mice), or 250 mg/kg bw/day (hamsters).

The environmental fate properties of propyl gallate will limit its likelihood of reaching either surface (drinking water) or ground water or bioaccumulating in the environment. Propyl gallate is expected to biodegrade in the environment with ultimate aerobic degradation estimated to be weeks and primary degradation in days. The primary route of exposure from its use as an antioxidant in pesticide formulations is expected to be through consumption of food to which this chemical has been applied. Migration to ground water drinking water sources is possible, but will be limited by its primary degradation and its moderate adsorption to soils and sediments; therefore, concern for exposures via drinking water is likely to be low. Dermal exposure from residential use of pesticide products containing propyl gallate is possible; however, inhalation exposure is not expected based on its nonvolatile nature.

Based on its rapid metabolism and excretion, low acute and chronic toxicity, and ready biodegradation in the environment, dietary (crops, meat,) and residential (dermal, inhalation) exposures of concern are not expected from the use of propyl gallate as an inert ingredient (antioxidant) in pesticide products.

Taking into consideration all available information, EPA has determined there is a reasonable certainty that no harm to any population subgroup will result from aggregate

exposure to propyl gallate when used as an inert ingredient in pesticide formulations when considering the 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 propyl gallate be maintained and considered reassessed as safe under section 408(q) of the FFDCA.

## X. Ecotoxicity and Ecological Risk Characterization

Propyl gallate may be considered moderately toxic to most aquatic organisms based on the ester and phenol SAR estimates. Available effects data from the Agency's Ecotox Database (http://www.epa.gov/ecotox) include several studies on agricultural crops (apples and sorghum) and one test on Zebra mussels. No statistically significant effects were noted to apples or sorghum. Zebra mussels were studied for 48 hours under static conditions. The 48h $EC_{50}$ was reported as 17.8 ppm for its ability to detach from its substrate (behavior).

Predicted acute toxicity values are approximately 40 parts per million (ppm) for fish 96h $LC_{50}$'s, and approximately 20 ppm to 200 ppm for aquatic invertebrate 48 h $EC_{50}$'s depending on structural class. These levels are unlikely to occur in surface waters as a result of the use of propyl gallate as in inert ingredient in pesticide products. Concentrations of propyl gallate at which chronic effects may occur tended to be lower than the predicted acute toxicity values; however, because of the potential for rapid biodegradation, repeated exposures would likely be necessary for effects to occur.

Propyl gallate 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 nonlisted species are not likely from the use of propyl gallate as an inert ingredient in pesticide products unless application rates exceed 10 or more pounds per acre on a yearly basis.

**References:**

Abdo, K.M. et al., No Evidence of Carcinogenicity of D-Mannitol and Propyl Gallate in F344 Rats or B6C3F$_1$ Mice, Fd Chem, Toxic., Vol 24, No. 10/11, pp. 1091-1097, 1986.

BIBRA Information Services Ltd., Toxicity Profile, Propyl Gallate, 1989.

Chen, Ssu-Ching and Chung, King-Thom, 2000, Mutagenicity and Antimutagenicity Studies of Tannic Acid and its Related Compounds, Food and Chemical Toxicology 38 (2000) 1-5.

CIR 1985, Final Report on the Safety Assessment on the Safety Assessment of Propyl Gallate, Journal of the American College of Toxicology, Volume 4, Number 3, 1985.

InChem 2004, http://www.inchem.org/documents/jecfa/jeceval/jec_1759.htm 2/6/2004.

NTP 1982, National Toxicology Program Technical Report Series No. 240, Carcinogenesis Bioassay of Propyl Gallate in F344 Rats and B6C3F$_1$ Mice (Feed Study), December 1982.

WHO Food Additives Series: 32, Toxicological Evaluation of Certain Food Additives and Contaminants, Gallates (Propyl, Octyl, and Dodecyl).

# APPENDIX A

## 21 CFR citations from the EAFUS (Everything Added to Food in the United States) Food Additive Database (http://www.cfsan.fda.gov/~dms/eafus.html 8/09/2005)

| 21 CFR § |
|---|
| **166.110** Margarine, maximum 0.02% individually or in combination with other preservatives |
| **172.615** Chewing Gum Base, not to exceed antioxidant content of 0.1% when used alone or in any combination. |
| **175.125** Indirect Food Additives: Adhesives and Components of Coatings: Pressure-sensitive adhesives |
| **175.300** Indirect Food Additives: Adhesives and Components of Coatings: Resinous and polymeric coatings |
| **175.380** Indirect Food Additives: Adhesives and Components of Coatings: Xylene-formaldehyde resins condensed with 4,4'-isopropylidenediphenol-epichlorohydrin epoxy resins |
| **175.390** Indirect Food Additives: Adhesives and Components of Coatings: Zinc-silicon dioxide matrix coatings |
| **176.170** Indirect Food Additives: Paperboard and Paperboard Components: Components of paper and paperboard in contact with aqueous and fatty foods. |
| **177.1010** Indirect Food Additives: Polymers: Acrylic and modified acrylic plastics, semirigid and rigid |
| **177.1210** Indirect Food Additives: Polymers: Closures with sealing gaskets for food containers |
| **177.1350** Indirect Food Additives: Polymers: Ethylene-vinyl acetate copolymers |
| **184.1660** Direct Food Substances Affirmed as Generally Recognized as Safe: Propyl Gallate |