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

OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES

February 27, 2006

ACTION MEMORANDUM

SUBJECT: Inert Reassessment – Tannin (CAS Reg. No. 1401-55-4)

FROM: Pauline Wagner, Chief Pauline Wagner 2/27/06
Inert Ingredient Assessment Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

Action: Reassessment of one exemption from the requirement of a tolerance for tannin. The reassessment decision is to maintain "as-is" the one exemption from the requirement of a tolerance.

Chemical: Tannin

CFR Citation				CAS Reg. No. 9CI Name
40 CFR §	Inert Ingredients	Limits	Uses	
180.920*	Tannin	(none)	Dispersing agent	1401-55-4 Tannins

*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 .

Use Summary: Tannin is approved for use as a dispersing agent in pesticide formulations applied to growing crops only under 40 CFR 180.920. Tannins also occur naturally in coffee and tea and nearly all wood and vegetation contain some form of tannin in the leaves, twigs, bark, wood, or fruit, including a variety of plants utilized for food and feed (food grains, fruits, wines, teas, and forages).

List Reclassification Determination: The current List Classification for tannin 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 tannin when used as a dispersing agent in pesticide formulations applied to growing crops only, the List Classification for tannin will change from List 3 to List 4B.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the exemption from the requirement of a tolerance for the inert ingredient tannin, CAS Reg. No. 1401-55-4 and with the List reclassification determination, as described above. I consider the one exemption established in 40 CFR part 180.920 [formerly 40 CFR 180.1001(d)], 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: 3/3/06

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC
SUBSTANCES

February 25, 2006

MEMORANDUM

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance For Tannin (CAS Reg. No. 1401-55-4)

FROM: Keri Grinstead
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 tannin (tannic acid). It will be referred to as tannin or tannic acid throughout this document. Tannin has one exemption from the requirement of a tolerance under 40 CFR 180.920 when used as an inert ingredient (dispersing agent) in pesticide formulations applied to growing crops only. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of tannin. The purpose of this document is to reassess the existing exemption from the requirement of a tolerance for residues of tannin when used as an inert ingredient (dispersing agent) in pesticide formulations as required under the Food Quality Protection Act (FQPA).

Executive Summary

This report evaluates the existing 40 CFR 180.920 exemption from the requirement of a tolerance for tannin when used as an inert ingredient (dispersing agent) in pesticide formulations applied to growing crops only.

Compounds considered to be tannins vary from simple phenols such as gallic acid to macromolecules with molecular weights between 500 and 3000. Tannins occur naturally in coffee and tea and nearly all wood and vegetation contain some form of tannin in the leaves, twigs, bark, wood, or fruit. Tannins can also be found in a variety of plants utilized for food and feed including food grains (sorghum, millets, barley, dry beans, faba beans, peas, carobs, pigeonpeas, winged beans, and legumes), fruits (apples, bananas, blackberries, cranberries, dates, grapes, hawthorns, peaches, pears, persimmons, plums, raspberries, and strawberries), and in wines, teas, and forages (Chung et al. 1998).

Tannic acid is affirmed as Generally Recognized as Safe (GRAS) by the Food and Drug Administration (FDA) for use as a direct food additive (with limitations) in numerous food and beverage products (see Table 2).

Tannin, orally administered to rabbits, was absorbed by the gastrointestinal tract, metabolized, and excreted within 24 hours. It has low acute, subchronic, and chronic oral toxicities in animal studies, and is nonmutagenic and noncarcinogenic. In a teratologic evaluation of tannic acid on rats and mice, no effects on nidation (implantation), maternal or fetal survival, or abnormalities in soft or skeletal tissues were seen at dosages of up to 135 mg/kg bw/day (mice) and 180 mg/kg bw/day (rats) for ten consecutive days during pregnancy. In addition, a three generation rat reproduction study resulted in a NOAEL of 60 mg/kg bw/day and a LOAEL of 117 mg/kg bw/day (lower pup weights at weaning), with no effects on fertility, gestation, viability, or lactation indices at any dose level. Suppressed reproductive activity was observed in mice kept on a continuous 8% tannic acid diet prior to and throughout the breeding cycle(s).

The environmental fate of tannin will limit its likelihood of reaching either surface (drinking water) or ground water or bioaccumulating in the environment. Tannin is expected to biodegrade in the environment with ultimate aerobic degradation estimated to be weeks and primary degradation estimated to be days. Migration to groundwater drinking water sources is possible in sandy soils, but will be limited in other soils by its rate of primary degradation and its strong sorption to soils and sediment and, therefore, exposures of concern via drinking water are likely to be low.

The primary route of exposure to tannin from its use as an inert ingredient in pesticide formulations is expected to be through consumption of food to which pesticide products containing tannin have been applied. Residential exposures (dermal and inhalation) of concern are not expected based on its use pattern, nonvolatile nature, and instability in the presence of light and oxygen. The exposure of the general population to tannin from its use in pesticide products is expected to be small in comparison to exposure from its natural occurrence in feed grains, wine, tea, fruits, and forage, and its use as an FDA-approved direct food additive in numerous food and beverage products. The rapid atmospheric oxidation, ready biodegradation, as well as the low toxicity and rapid metabolism and excretion of tannin further decrease the likelihood of dietary exposures of concern from tannin as an inert ingredient in pesticide formulations.

Tannin is considered to be moderately toxic to practically nontoxic to aquatic organisms. Ecological concerns for listed and nonlisted species are not likely from its use as an inert ingredient in pesticide formulations based on application rates of less than 10 pounds per acre.

Taking into consideration all available information on tannin, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to tannin when used as an inert ingredient (dispersing agent) in pesticide formulations 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 one exemption from the requirement of a tolerance established for residues of tannin, 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 tannin, an inert ingredient used as a dispersing agent in pesticide formulations. Tannin has one exemption from the requirement of a tolerance under 40 CFR 180.920 when applied to growing crops only.

According to and/or cited by Rashid et al. (1985), "Tannic acid, the commercial term for a mixture of large gallotannins, trigallic, m-digallic, and gallic acid (King and Pruden 1970) is extracted from plant material." "Gallotannins are large polyphenolic compounds consisting of glucose esterified to gallic acid" and "occur in 18% of all dicotyledenous plants and play important roles in defense against attack by bacteria, fungi, or herbivores (Swain 1979)."

Compounds considered to be tannins vary from simple phenols such as gallic acid to macromolecules with molecular weights between 500 and 3000. Tannins occur naturally in coffee and tea and nearly all wood and vegetation contain some form of tannin in the leaves, twigs, bark, wood, or fruit. Tannins can also be found in a variety of plants utilized for food and feed including food grains (sorghum, millets, barley, dry beans, faba beans, peas, carobs, pigeonpeas, winged beans, and legumes), fruits (apples, bananas, blackberries, cranberries, dates, grapes, hawthorns, peaches, pears, persimmons, plums, raspberries, and strawberries), and in wines, teas, and forages (Chung et al. 1998).

There are two types of tannins: condensed tannins and hydrolyzable tannins. Condensed tannins are those derived from flavonols and contain little or no carbohydrate. Hydrolyzable tannins are esters of sugar hydrolyzed by acids, alkalis and enzymes into glucose or other polyhydric alcohols and phenolic acids; they are further subdivided into two groups based on the phenolic acids they contain (i.e., gallotannins or ellagitannins) (International Agency for Research on Cancer (IARC) 1976). According to IARC "tannic acid is the astringent or tanning principle occurring in the wood, bark, fruit, leaves, and roots of a large number of plants." The Environmental Protection Agency's Substance Registry System (SRS) lists the following synonyms for tannin: tannic acid, tannins, quebracho wood extract, quebracho extract, Chinese tannin, glycerite, digallic acid, gallotannic acid, gallotannin, and penta NM digalloyl glucose.

II. Use Information

A. Pesticide Uses

Tannin is approved for use as a dispersing agent in pesticide formulations applied to growing crops only. The exemption from the requirement of a tolerance for its use in pesticide products applied to growing crops only is provided in Table 1 below.

Table 1. Pesticide Uses

CFR Citation				CAS Reg. No. 9CI Name
40 CFR §	Inert Ingredients	Limits	Uses	
180.920*	Tannin	(none)	Dispersing agent	1401-55-4 Tannins

*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

Tannic acid is affirmed as Generally Recognized as Safe (GRAS) by the Food and Drug Administration (FDA) for use as a direct food additive (with limitations) as listed in Table 2. below. According to the 1996 Merck Index 12th Edition, uses of tannic acid include: as a mordant in dyeing; in the manufacture of ink; sizing paper and silk; printing fabrics; with gelatin and albumin for the manufacture of imitation horn and tortoise shell; tanning; clarifying beer or wine; in photography; as a coagulant in rubber manufacturing; in the manufacture of gallic acid and pyrogallol; and as a reagent in analytical chemistry.

Table 2. Direct Food Additive Uses/Limitations

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)		
173.310	Secondary Direct Food Additives Permitted in Food for Human Consumption – boiler water additive	
184.1097	Direct Food Substances Affirmed as Generally Recognized as Safe Tannic Acid – for use in:	Maximum level of use in food (as served) (percent)
	– baked goods and baking mixes	0.01
	– alcoholic beverages	0.015
	– nonalcoholic beverages and beverage bases	0.005
	– gelatins, puddings, and fillings	0.005
	– frozen dairy desserts and mixes, soft candy	0.04
	– hard candy, cough drops	0.013
	– meat products	0.001
	– rendered animal fat	in accordance with 9 CFR 318.7

III. Physical and Chemical Properties

Table 3. Physical and Chemical Properties

Commercial Reagent–Grade Tannic acid (CAS Reg. No. 1401-55-4)		
Parameter	Value	Source
Molecular formula	Usually given as $C_{76}H_{52}O_{46}$	IARC 1976
Molecular Wt.	1701.2	IARC 1976

Commercial Reagent–Grade Tannic acid (CAS Reg. No. 1401-55-4)		
Parameter	Value	Source
Color/Form	Yellowish-white to light brown, amorphous, bulky powder or flakes of spongy masses	IARC 1976
Solubility	1g dissolves in 0.35 mL of water	IARC 1976
Stability	Gradually darkens on exposure to air and light; when heated to approximately 210-215° C, it decomposes primarily into pyrogallol and carbon dioxide; aqueous solutions decompose on heating.	IARC 1976
Reactivity	Insoluble precipitates are formed with albumin, starch, gelatin and most alkali and metallic salts; it has been reported to catalyse the formation of nitrosodiethylamine.	Walker et al., 1975 as cited in IARC 1976

IV. Hazard Assessment

A. Hazard Profile

This hazard assessment was developed primarily using a 1976 IARC report on tannic acid, The Merck Index (12th Edition), a Joint FAO/WHO Expert Committee on Food Additives (JECFA) report on tannin, Agency databases, and various studies/articles.

Tannin has low acute, subchronic, and chronic oral toxicities in animal studies, and is nonmutagenic and noncarcinogenic. In developmental studies, no effects on nidation (implantation), maternal or fetal survival, or abnormalities in soft or skeletal tissues were seen at dosages of up to 135 mg/kg (mice) and 180 mg/kg (rats). In addition, a three generation rat reproduction study resulted in a NOAEL of 60 mg/kg bw/day and a LOAEL of 117 mg/kg bw/day (lower pup weaning weights), with no effects on fertility, gestation, viability, or lactation indices at any dose level. Reduced fecundity was observed in mice fed a continuous diet containing 8% both prior to and throughout the breeding cycle(s). The exposure of the general population to tannin from its use in pesticide products is expected to be small in comparison to exposure from its natural occurrence in feed grains, wine, tea, fruits, and forage, and its use as a direct food additive in numerous food and beverage products.

B. Metabolism and Pharmacokinetics

Tannins occur naturally in coffee and tea and nearly all wood and vegetation contain some form of tannin in the leaves, twigs, bark, wood, or fruit. Tannins can also be found in fruits, wines, teas and in a variety of plants utilized for food and feed including food grains and forages (Chung et al. 1998).

"Korpassy et al. 1951, found an increased concentration of tannic acid in the blood of rabbits and dogs given tannic acid by stomach tube, with a maximum level after three hours. Absorption of tannic acid from the colon, as shown by rising blood levels, was demonstrated in rabbits, sheep, goats, rats and dogs" (as cited in IARC 1976). According to Dollahite et al., 1962, in rabbits, tannic acid was rapidly absorbed from the

gastrointestinal tract into the bloodstream and rapidly detoxified or excreted. "Tannic acid and gallic acid would possibly be combined by the proteins in the gastrointestinal tract, thereby reducing the quantity available for uptake" and "in rabbits not given a lethal dose of tannic acid, the serum tannic acid level is completely metabolized or eliminated within 24 hours."

According to Chung et al. (1998), "Tannins form complexes with proteins, starch, and digestive enzymes to cause a reduction in nutritional values of foods. They can cause a browning reaction in foods through the action of polyphenol oxidase by darkening reactions adversely affecting the acceptability of such foods." The antinutritional effects seem to be predominantly related to condensed tannins probably due to hydrolyzable tannins being present only in trace amounts in commonly consumed foods. "Tannins are of nutritional concern for people whose diets depend largely on crops with high tannin content. It is not advisable to ingest a large quantity of high tannin-containing foods; tannins affect protein absorption and metabolism." "Animals fed on tannin-free diets had higher feed consumption and weight gains, compared with those fed on a diet with endogenous tannin or tannin supplementation for an extended period of time." "Rats could tolerate up to 5% tannins mixed in a good ration. However, a much higher content of tannins caused a marked growth depression." "Tannins are known to affect the utilization of vitamins and minerals."

C. Toxicological Data

Acute Oral

Based on the oral LD_{50} values, tannic acid is of low acute oral toxicity when administered to rats.

Table 4. Rat Intragastric LD_{50} Values

Rat Intragastric LD_{50} Values ("Food and Drug Res. Lab. 1964, 1965, 1967, as cited in JECFA 1970")	
Plant Source of Tannin	LD_{50}
Aleppo	1550 mg/kg
Tara	3700 mg/kg
Chinese	2800 mg/kg
Sicilian sumac	2650 mg/kg
Douglas fir	7500 mg/kg

Subchronic Oral Toxicity

According to JECFA (Joint FAO/WHO Expert Committee on Food Additives) (1970), seven groups of male and female rats received 0, 8, 80, or 800 mg/kg bw/day of Aleppo or tara tannin in their diet for twelve weeks. No significant changes in body

weight, food intake and food utilization, liver and kidney weights, or gross and histopathology were seen (Food and Drug Res. Lab. 1964). "Similar studies at these same levels using Chinese tannin (Food and Drug Res. Lab. 1965), Sicilian sumac tannin (Food and Drug Res. Lab. 1967), and Douglas fir tannin (Food and Drug Res. Lab. 1967) at these same levels produced comparable findings."

Chronic Oral Toxicity

No adverse effects (as judged by survival, growth, food consumption, hematology, organ weights and gross and microscopic pathology) were noted in five groups of male and female rats dosed with tannin (from Peruvian tara) at dietary levels of 0, 0.117, 0.125, 0.234, or 0.25% (equivalent to 58.5, 62.5, 117.0, and 125 mg/kg bw/day) for two years (Rosner-Hixon Lab, 1965 as cited in JECFA 1970).

Five groups of male and female dogs received 0.0, 0.117, 0.125, 0.234, or 0.25% tannin (equivalent to 58.5, 62.5, 117.0, and 125 mg/kg bw/day respectively) (from Peruvian tara) in their diets for two years. No ill effects on behavior, food consumption, hematology, organ function tests, or on organ weights and gross microscopic pathology were noted at any dose level (Rosner-Hixon Lab, 1965 as cited in JECFA 1970).

Mutagenicity

In Ames testing using *Salmonella typhimurium* strains TA98, TA100, and TA1535, tannic acid was shown to be nonmutagenic both with and without activation using S-9 mix from rat and woodchuck liver (Rashid et al. 1985).

According to Chung et al. (1998), mutagenicity testing of tannic acid from tea was shown to be nonmutagenic to *S. typhimurium* strains TA98, TA100, TA1535, and TA1538 with or without metabolic activation and those tannin fractions did not increase tumor incidence in gavage-fed Swiss mice. In addition, "Tannic acid was found not to be clastogenic to germ cells of male *Drosophila melanogaster.*"

Carcinogenicity

"A recent study by Onodera et al. using F344 rats of both sexes showed that tannic acid given *ad libitum* as 0.25 or 0.50% in distilled water for up to two years did not significantly increase the incidence of any tumor. Thus, tannic acid has no carcinogenic potential in F344 rat or modifying effects on development of spontaneous tumors" (Chung et al. 1998).

Tannin isolated from bracken fern was determined to be noncarcinogenic in a 72 week study of rats fed a basic diet containing 0.1% tannin for weeks 0-3, followed by 0.2% tannin for weeks 3-22, and then 0.4% tannin for weeks 22-72 (cumulative total tannin dose of 22,500 mg/rat) (Pamucku et al. 1980).

Developmental/Reproductive Toxicity

Female mice were dosed via oral intubation with tannic acid at 1.35, 6.27, 29.1, or 135 mg/kg on days 6-15 of gestation. The final report concluded that "administration of up to 135 mg/kg (body weight) of the test material to pregnant mice for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues for the test groups did not differ from the number occurring spontaneously in the sham-treated controls" (NTIS 1975).

Female rats were dosed via oral intubation with tannic acid at 1.8, 8.4, 38.8, or 180 mg/kg on days 6-15 of gestation. The final report concluded that "administration of up to 180 mg/kg (body weight) of the test material to pregnant rats for 10 consecutive days had no clearly discernible effect on nidation or on maternal of fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls" (NTIS 1975).

A three-generation reproduction study was conducted on male and female rats fed Peruvian tara tannin at dietary levels of 0.0 or 0.234% (117 mg/kg bw/day) and at 0.0, 0.058 (29 mg/kg bw/day), or 0.117% (60 mg/kg bw/day). No effects upon fertility, gestation, viability, or lactation indices were seen at any dose level; however, pups in the 0.234% (117 mg/kg bw/day) dosing group had significantly lower weights at weaning. The NOAEL for this study was 0.117% (60 mg/kg bw/day) (Rosner-Hixon Lab. 1969 as cited in JECFA 1970).

Peaslee and Einhellig (1973b) reported that "White mice fed a continuous diet of 8% tannic acid in laboratory chow produced litters of smaller number, slower growth rates, and lower body-weight plateau." In addition, "Females on this tannic acid diet required a longer time to become impregnated." Mice were fed 8% tannic acid diets both prior to and throughout the breeding cycle(s).

D. Special Consideration for Infants and Children

Results of developmental studies showed no effects on nidation (implantation), maternal or fetal survival, or abnormalities in soft or skeletal tissues were seen at dosages of up to 135 mg/kg (mice) and 180 mg/kg (rats). In addition, a three generation rat reproduction study resulted in a NOAEL of 60 mg/kg bw/day and a LOAEL of 117 mg/kg bw/day (lower pup weights at weaning), with no effects on fertility, gestation, viability, or lactation indices at any dose level. The use of tannin as an inert ingredient in pesticide formulations would not contribute greatly to the natural levels present in foodstuffs, which is expected to be orders of magnitude less than the levels seen in reproductive/developmental studies. Based on this information, as well as its natural occurrence as a normal component in the human diet and its long history of use as a direct food additive in numerous foodstuffs, there is no concern, at this time, for increased sensitivity to infants and children to tannin from its use as an inert ingredient

(dispersing agent) 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[1]

There are no available measured data, therefore, based on the estimated physical-chemical and environmental transformation properties, tannin is not likely to persist in aerobic environments, leach to ground water except in sandy soils or through preferential plow, or bioconcentrate/bioaccumulate in the environment. Tannin is predicted to be readily biodegradable with ultimate aerobic degradation estimated to be weeks and primary degradation estimated to be days. Tannin is slightly to moderately soluble in water, nonvolatile, and exhibits strong sorption to very strong sorption to soil (Log Koc=4.912). Leaching to groundwater is likely in sandy or porous soils, however this is mitigated in other soils due to biodegradation and sorption. The potential for tannin to volatilize from surface waters is low and it undergoes rapid atmospheric oxidation in the presence of hydroxyl radicals with a half-life of 0.96 hours if volatilization from soils or water does occur.

While it is possible that tannin used for agricultural purposes could reach drinking water (from surface water), the environmental contribution from the use of tannin in pesticide products is likely to be small in comparison to the tannin that is found naturally in the environment due to its natural occurrence in nearly all wood and vegetation. Additionally, its instability in the presence of light and oxygen and rapid biodegradation further decrease the likelihood of environmental and drinking water concentrations of concern from its use as an inert ingredient in pesticide products.

VI. Exposure Assessment

For the general population, the majority of exposure to tannin(s) comes from its natural occurrence in coffee, wine, tea, food grains, fruits, and from its use as a direct food additive in numerous food and beverage products. It is affirmed as GRAS by the FDA as a direct food additive (see Table 2).

Tannin is approved for use as a dispersing agent in pesticide formulations applied to growing crops only. The primary route of exposure from its use in pesticide products is expected to be through consumption of food to which pesticide products containing tannin have been applied. Dermal exposure from residential uses of pesticide products containing tannin is possible; however, inhalation exposure is unlikely based on its nonvolatile nature.

Migration of tannin to ground water (from surface water runoff) is possible, but will be limited by its low solubility in water, strong sorption to soils and ready biodegradation, therefore, exposures of concern from drinking water are likely to be low.

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[1] all annotated values were calculated from the Agency's EpiSuite program at http://www.epa.gov/opptintr/exposure/docs/EPISuitedl.htm

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 gardens, lawns, or buildings (residential and other indoor uses).

For tannin, 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 tannin when used as an inert ingredient in pesticide formulations.

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 finding as to tannin and any other substances, and tannin does not appear to produce a toxic metabolite produced by other substances. For the purposes of these tolerance actions, therefore, EPA has not assumed that tannin 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/.

Human Health Risk Characterization

Tannin is approved for use as a dispersing agent in pesticide formulations applied to growing crops only. Tannin has low acute, subchronic, and chronic oral toxicities in animal studies, and is nonmutagenic and noncarcinogenic. In developmental studies, no effects on nidation (implantation), maternal or fetal survival, or abnormalities in soft or skeletal tissues were seen at dosages of up to 135 mg/kg (mice) and 180 mg/kg (rats). In addition, a three generation rat reproduction study resulted in a NOAEL of 60 mg/kg bw/day and a LOAEL of 117 mg/kg bw/day (lower pup weaning weights), with no effects on fertility, gestation, viability, or lactation indices at any dose level. Reduced fecundity was observed in mice fed a continuous diet containing 8% both prior to and throughout the breeding cycle(s). The exposure of the general population to tannin from its use in pesticide products is expected to be small in comparison to exposure from its natural occurrence in feed grains, wine, tea, fruits, and forage, and its use as a direct food

additive in numerous food and beverage products. Considering its rapid atmospheric oxidation, ready biodegradation, as well as its low toxicity and rapid metabolism and excretion, dietary exposures of concern from the use of pesticide products containing tannin are not anticipated. Residential exposures of concern are not expected from the use of tannin as an inert ingredient (dispersing agent) in pesticide formulations.

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 tannin when used as an inert ingredient in pesticide formulations when considering the dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the one exemption from the requirement of a tolerance established for residues of tannin be maintained and considered reassessed as safe under section 408(q) of the FFDCA.

X. Ecotoxicity and Ecological Risk Characterization

Tannins may be considered moderately toxic to practically nontoxic to most aquatic organisms based on measured effects data located in the Agency's Ecotox Database (http://www.epa.gov/ecotox/) and on the ester and phenol SAR (Structure Activity Relationship) estimates.

Measured effects data for fish indicate 48h to 96h $LC_{50's}$ are on the order of several mg/L to >100 mg/L depending on species and test conditions. Aquatic invertebrate data is more limited, but indicate effects levels for population and behavior in the low mg/L range (e.g., *Daphnia magna* effects level for behavior of <26 mg/L). A single study on the bull frog for 12 hours under static conditions was inconclusive at concentrations up to 1000 mg/L. Plant effects data for both aquatic (blue-green algae) and terrestrial (agricultural crop) species reported no adverse responses up to the test dose for terrestrial plants (note: test concentrations were not verified in the terrestrial plant studies) and a decrease in algae population at 100 μmoles. No chronic effects data were reported in Ecotox.

Depending on structural class (esters or phenols), predicted acute toxicity values are approximately: 1400-2100 parts per million (ppm) for fish 96h $LC_{50's}$, 260-49000 ppm for daphnid 48h $LC_{50's}$, and 100-27500 ppm for green algae 96h $EC_{50's}$. These levels are unlikely to occur in surface waters as a result of the use tannin as an inert ingredient in pesticide formulations. Chronic effects estimates range from approximately 70 mg/L of algae based on the ester SAR class and 330 mg/L for fish based on the phenol SAR class. Even with frequent applications in agricultural or commercial/residential settings at applications in excess of 10 pounds per acre, concentrations in surface water as a result of pesticide use is unlikely to reach effects thresholds. Using mammalian data as a surrogate for terrestrial organisms, tannin is unlike to result in adverse effects from pesticide uses.

Tannin is not expected to bioaccumulate in the environment, therefore, based on potential exposures and estimated toxicity to aquatic and terrestrial organisms (using

available rat and mouse data as surrogate for all terrestrial animals), ecological concerns for listed and nonlisted species are not likely from the use of tannin as an inert ingredient in pesticide products.

References:

Chung, King-Thom; Wong, Tit Yee; Wie, Cheng-I; Huang, Yao-Wen; and Lin, Yuan; Tannins and Human Health: A Review, *Critical Reviews in Food Science and Nutrition*, 38(6):421-464 (1998).

Dollahite, James W.; Pigeon, Robert F.; and Camp, Bennie J.; The toxicity of Gallic Acid, Pyrogallol, Tannic Acid, and *Quercus havardi* in the Rabbit, Am. J. Vet. Res., Nov., 1962, **23**, 97, pp 1264-1267.

Environmental Protection Agency, EpiSuite program (V. 3.12), http://www.epa.gov/opptintr/exposure/docs/EPISuitedl.htm)

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