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

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

February 22, 2008

MEMORANDUM

SUBJECT: Decision Document for Petition Number 6E7062;
Ferric Citrate (CAS Reg. No. 2338-05-8)

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OVERVIEW

The Shepherd Chemical Company is requesting that ferric citrate be exempt from the requirement of tolerance in or on raw agricultural commodities under 40 CFR 180.910 when these substances are used as inert ingredients in pesticide formulations. After considering the available toxicity and exposure data, EPA recommends that the requested exemption from the requirement of tolerance be granted.

EXECUTIVE SUMMARY

The Shepherd Chemical Company is requesting an exemption from tolerance for ferric citrate (CAS Reg. No. 2338-05-8). The toxicity data are from the published literature and an EPA Reregistration Eligibility Document (RED). For exposure, standard models were used along with available data.

In summary, ferric citrate has low acute oral toxicity. In subchronic and chronic toxicity in rodents, no effects were noted. Ferric citrate has not been shown to be mutagenic or carcinogenic. Finally, no developmental and reproductive effects have been shown. Based on this information there is no concern, at this time, for increased sensitivity to infants and children to ferric citrate when used as an inert ingredient in pesticide formulations. For the same reason, 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.

Ferric citrate will be used as an inert ingredient in pesticide formulations applied to raw agricultural commodities. In addition to exposure through the pesticide application, individuals may be exposed to iron through their diet (iron is an essential nutrient); and as a pharmaceutical (to treat iron deficiency). Application of pesticide formulations containing ferric citrate is not expected to result in residues of concern; modeled exposure estimates are low. Iron is an essential nutrient that, by definition, must be obtained through the diet. Foods rich in iron include: beef, chicken, oysters, soybeans, lentils, and spinach. Iron occurs naturally in ground and surface waters. Any contribution from application of ferric citrate is expected to be minimal. Considering the environmental fate of related iron compounds, ferric citrate is not expected to be mobile but rather will remain mostly in soil where it is not expected to contribute significantly to the chemistry and fate of the compounds existing naturally in the environment. As a pharmaceutical, about a quarter of the U.S. population is estimated to ingest iron daily to ensure that they are ingesting adequate amounts of iron.

Taking into consideration all available information on ferric citrate, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to ferric citrate when used as an inert ingredient in pesticide formulations when considering dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, the exemption from the requirement of a tolerance requested by the petitioner, The Shepherd Chemical Company, for residues of ferric citrate, can be considered assessed as safe under section 408(q) of FFDCA (or the Federal Food, Drug, and Cosmetic Act).

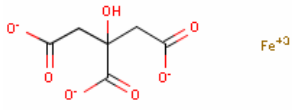
I. BACKGROUND

Under a Notice of Filing (NOF) published on June 7, 2006 (71 FR 32955) the Shepherd Chemical Company is requesting that ferric citrate be exempt from the requirement of tolerance in or on raw agricultural commodities when used as an inert ingredient in pesticide formulations. That is, the Shepherd Chemical Company is requesting that ferric citrate be exempt from the requirement of tolerance under 40 CFR 180.910 as a stabilizing agent. No comments were received in response to the NOF.

II. PHYSICAL AND CHEMICAL PROPERTIES

"Ferric Citrate occurs as brown granules or as thin, transparent, garnet red scales. It is more readily soluble in hot water than in cold, but it is insoluble in alcohol" (Committee on Food Chemicals Codex 2003). It appears to decompose on heating or exposure to light. Some other physical and chemical properties are provided in Table 1:

Table 1. Physical and Chemical Properties of Ferric Citrate

Parameter	Value	Source
Structure		NIH 2004
CAS #	2338-05-8	NIH 2004
Molecular Weight	244.943	NIH 2004
Common Names	iron citrate; iron(III) citrate	NIH 2004

III. HUMAN HEALTH ASSESSMENT

Iron is one of the most common elements on Earth and it is essential to nearly all known organisms. It can exist in oxidation states ranging from -2 to +6 but in biological systems three states are commonly found: ferrous (+2); ferric (+3); and ferryl (+4) (IOM 2001). The iron of ferric citrate is in the +3 oxidation state.

Iron in the body is bound to proteins such as transferrin, hemoglobin, myoglobin, ferritin, and hemosiderin; most of the iron in the body, 60 to 70 percent, is found in the hemoglobin molecule. Ingested iron is absorbed from the gastrointestinal (GI) tract and a small amount is excreted. An adult male needs to absorb only about 1 mg/day to maintain iron balance. In total, there is about 3 to 5 g of iron in the body. Within the body the disposition of iron is regulated by a complex mechanism to maintain homeostasis which involves transfer among the liver, spleen, bone marrow, and blood. (Klaasen et al 1986; IOM 2001)

Iron is an essential nutrient; it plays a vital role in the transport of oxygen throughout the body. Too little may result in anemia—iron deficiency anemia is the most common nutritional deficiency in the world, resulting in fatigue and impaired cognitive development and productivity. However, the prevalence of iron deficiency in the United States is low (NRC 1989). Too much iron can cause adverse effects. (Klaasen et al 1986; IOM 2001) Klaasen et al (1986) point out that "acute iron toxicity is nearly always due to ingestion of iron-containing medicines…" and that chronic iron toxicity (iron overload) is actually a more common problem. Iron overload can result from health-based problems (need for blood transfusions; idiopathic hemochromotosis) or from excess dietary iron (Klaasen et al 1986). The Institute of Medicine (IOM), in developing its Dietary Reference Intakes (DRI), determined an upper level of exposure to iron; it is based on GI manifestations (IOM 2001).

Acute Toxicity

No acute toxicity studies per se were identified for ferric citrate. In 2002 the Agency reassessed the tolerance exemptions for the mineral acids and their salts (USEPA 2002). Among the chemicals assessed were the iron sulfates. Acute toxicity values included:

[1]oral LD_{50} rat:	1,487 to 2,102 mg/kg
[2]oral LD_{50} mice:	1,520 mg/kg
[1]dermal LD_{50} rabbit:	>2,000 mg/kg
[1]inhalation LC_{50} rat:	>1.10 mg/L
[1]Eye Irritation:	corrosive
[1]Dermal Irritation:	corrosive
[1]Dermal Sensitization:	negative

[1]Conducted with ferric (III) sulfate; [2]Conducted with iron (II) heptahydrate

IOM (2001) discusses reports of acute toxicity resulting from overdoses of medicinal iron, especially in young children. Accidental iron overdose is the most common cause of poisoning deaths in children under six years of age in the U.S. The severity of iron toxicity is related to the amount of elemental iron absorbed. Gastrointestinal manifestations occur following the ingestion of 20 mg/kg bw and systemic toxicity may occur following the ingestion of 60 mg/kg bw. Vomiting and diarrhea characterize the initial stages of iron intoxication while later systemic effects can include those involving the heart, central nervous system, kidney, liver, and blood. The Institute of Medicine (IOM 2001) reports that in studies with adults, GI effects were seen at 50 mg/day of elemental iron; this finding is supported by other studies showing similar effects.

Subchronic Toxicity

Inai et al (1994) administered ferric citrate in the drinking water of male and female mice at doses of: 1; 0.5; 0.25; 0.12; or 0.06% (which is equivalent to 0; 600; 1,200; 2,500; 5,000; or 10,000 ppm) for 13 weeks. The investigators determined that the maximum tolerated dose is 0.12%. No "specific findings induced by the oral administration of ferric citrate could be detected.

Mutagenicity

Ishidate et al (1984) conducted the Ames test (with *S. typhimurium* strains TA92, TA 1535, TA100, TA1537, TA94, and TA98) and chromosomal aberration testing (with Chinese hamster fibroblasts). In the Ames test using 25 mg/plate of ferric citrate (the maximum dose), no significant increases in the number of revertant colonies were detected in any *S. typhimurium* strains. In the chromosomal aberration testing using 0.5 mg/mL(the maximum dose), polyploidy was observed in 3% of the cells after 48 hours and structural aberration was observed in 1% of the cells after 48 hours; the investigators concluded that these results were negative for chromosomal aberration.

Chronic Toxicity

Ferric citrate was orally administered at concentrations of 0.12% (maximum tolerated dose), 0.06%, or 0% in the drinking water to male and female $B6C3F_1$ mice (for males, 0.12% ferric citrate in drinking water is equivalent to 0.22 mg/kg/day and 0.06% is equivalent to 0.10 mg/kg/day; for females, 0.12% ferric is equivalent to 0.16 mg/kg/day and 0.06% is equivalent to 0.07 mg/kg/day). These concentrations were chosen on the basis of the results of the subchronic testing. Treatment was continued for 13 weeks. There was no significant difference between treated and control groups in the tumor incidence or in the distribution of different types of tumor. Thus the long-term oral administration of ferric citrate to mice did not yield any evidence of chronic toxicity or tumorigenicity. (Inai et al 1994)

Developmental and Reproductive Toxicity

To determine if toxic fetal serum iron levels are reached when maternal serum iron concentrations rise above what the body can homeostatically maintain, investigators (Curry et al 1990) dosed pregnant sheep with toxic doses of iron. Specifically, four gravid ewes were dosed with ferric chloride at 2 mg/kg/bw via intravenous administration over 60 minutes; this route was chosen over the oral route because only a small amount of iron is absorbed from the GI tract after overdose. A significant rise was observed in the maternal serum iron concentration but not in that of the fetuses. The investigators concluded that the fetus is protected from elevated maternal serum iron concentrations during the third trimester of pregnancy, a period when the fetus acquires most of the iron that it needs during the gestational period.

Summary

From what is known about the sulfates of iron (as opposed to the citrate), it appears that ferric citrate is not acutely toxic via the oral route. In subchronic toxicity using mice, no effects were noted at the maximum tolerated dose, which was 0.12% ferric citrate in distilled water (this is approximately equivalent to 0.17 mg/kg/day). In chronic toxicity testing, no effects were seen at 0.22 mg/kg/day. Ferric citrate has not been shown to be mutagenic or carcinogenic. Finally, no developmental and reproductive effects have been shown.

Based on this information there is no concern, at this time, for increased sensitivity to infants and children to ferric citrate when used as an inert ingredient in pesticide formulations. For the same reason, 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.

IV. Environmental Fate Characterization and Drinking Water Considerations

Environmental Fate

In 1993 (USEPA 1993) the Agency assessed the environmental fate of the iron sulfates. Because specific information on the fate of iron citrate is not available, the Agency is relying on the iron sulfate assessment (USEPA 1993) to describe the fate of the iron moiety of iron citrate. This is reasonable given that the concentration of iron citrate in the formulation will be low (1%) and the iron moiety of the sulfate salts and citrate is expected to behave in a similar fashion. Provided below is the summary and conclusion for the environmental fate assessment for the iron salts (USEPA 1993):

> In summary, the fate and transport of Fe(II) and Fe(III) salts in the environment is dominated by three major processes: (1) the pH-redox potential dependent oxidation of Fe(II) to Fe(III); (2) the formation of insoluble oxides and hydroxides that are also well known components of soils; and (3) the distinct surface chemistry of the oxides and hydroxides of iron that control the adsorption of anions, cations and organic material or the adsorption of iron species onto the surfaces of mineral and organic components of soils, contributing to the aggregation of soil particles into larger units.
>
> In terrestrial environments, the use of Fe(II) and Fe(III) sulfates is expected to produce iron oxides and hydroxides that are no different from the iron oxides and hydroxides found in soils and which are responsible for their brown and red colors. Although certain bacteria can reduce Fe(III) to the more mobile Fe(II), reoxidation and reprecipitation to Fe(III) oxides and hydroxides will rapidly immobilize any free Fe(II) that may form.
>
> Therefore, the use of the iron salts as herbicides to control moss in residential outdoor ornamentals (herbaceous and woody plants; lawns and turf) or as fertilizers to correct chlorosis in plants is not expected to contribute significantly to the chemistry and fate of the compounds existing naturally in the environment.

So, based on what is known on the salts of iron in the environment, EPA does not expect that iron citrate will pose environmental risks of concern.

Drinking Water

Iron occurs naturally in ground and surface waters. The Agency sets nonenforceable standards for certain contaminants that may cause cosmetic effects (such as skin or tooth discoloration) or aesthetic effects (such as taste, odor, or color) in drinking water. EPA recommends secondary standards to water systems but does not require systems to comply. However, states may choose to adopt them as enforceable standards. These standards are referred to as National Secondary Drinking Water Regulations. For iron, the standard is 0.3 mg/L.

Iron concentrations in groundwater have been reported to range <0.5 to 100 mg/L; higher values have been found in the absence of oxygen and in the presences of organic matter. In surface waters, iron concentrations can vary widely, ranging from 61 to 2,680 mg/L. (NIH 2005b)

V. Aggregate Exposure Assessment

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 (ground water or surface water) and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

EPA does not have information available to assess the potential for exposure to ferric citrate in consumer products. Nevertheless, given: the natural and ubiquitous occurrence of iron-containing compounds in the environment; iron's known role in human physiology; and its presence in various foods such as beef, soybeans, lentils, and spinach (NIH 2005a), it is unlikely that residential exposures of concern would result from the use of ferric citrate in nonpesticide products and as an inert ingredient in pesticides. Therefore, no further aggregate assessment is necessary.

EPA estimated dietary exposures for use of ferric citrate as an inert ingredient using a dietary exposure screening model referred to as DEEM™ (USEPA 2007b). DEEM™, or Dietary Exposure Evaluation Model, is a generic screening model that assumes that the inert ingredient is used on all commodities and that 100 percent of crops are treated with the inert ingredient. Further, it assumes finite residues for every consumed commodity (including meat, milk, poultry, and eggs) included in the model. DEEM™ does not include a weight fraction input, but instead is based on a group of active ingredients that are typically found in agricultural food-use products at concentrations ranging from >50% to 100% of the formulation. Provided in Table 2 are the estimated generic chronic exposures for the U.S. population and several subgroups along with the ferric citrate exposures (which happen to be the same as the generic

exposures[1]). Please note that these estimates are unrefined and very conservative in nature.

Table 2. Estimated Chronic Dietary Exposure for Ferric Citrate Use in Glyphosate (USEPA 2007)

Population Subgroup[1]	Estimated Exposure (mg/kg/day)[2]		
	Generic	Ferric Citrate	Ferric Citrate as 1% in Formulation
U.S. Population (total)	0.120	0.120	0.0012
All infants (<1 year)	0.245	0.245	0.0025
Children (1-2 years)	0.422	0.422	0.0042
Children (3-5 years)	0.310	0.310	0.0031
Children (6-12 years)	0.174	0.174	0.0017
Youth (13-19 years)	0.100	0.100	0.0010
Adults (20-49 years)	0.087	0.087	0.0009
Adults (50+ years)	0.086	0.086	0.0009
Females (13-49 years)	0.087	0.087	0.0009

[1]Only representative population subgroups are shown.
[2]Exposure estimates are based on highest tolerance-level residues of high-use active ingredients for all food forms including meat, milk, poultry, and eggs.

In addition to exposure from use in pesticides, individuals are exposed to iron through the diet. Iron is an essential nutrient that, by definition, must be obtained through the diet. Foods rich in iron include: beef, chicken, oysters, soybeans, lentils, and spinach (NIH 2005a). To ensure health, The National Academy of Sciences (NAS) recommends that adults consume 8 mg of iron per day (or about 0.11 mg/kg/day); this is the Recommended Daily Allowance or RDA (IOM 2001). Data from nationally representative U.S. surveys show that the median daily intake of dietary iron by men is about 16 to 18 mg/day (or 0.23 to 0.26 mg/kg/day) and women about 12 mg/day (or 0.17 mg/kg/day). (IOM 2001) In addition to food, cookware containing iron, such as stainless steel or cast iron, can be a source of iron in the diet (NIH 2005b).

Finally, salts of iron (e.g., ferrous sulfate) are used as pharmaceuticals. About 21 to 25 percent of women and 16 percent of men were reported to take a daily iron supplement; on average it is estimated to contain about 1 mg of iron/day (or 0.014 mg/kg/day). (IOM 2001)

VI. 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."

[1]The generic exposures and ferric citrate exposures are the same because it was assumed that ferric citrate would be used at a concentration of 100%. If a lower concentration of ferric citrate were assumed, the generic exposures would be adjusted accordingly.

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 ferric citrate and any other substances and, this material does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that ferric citrate 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/.

VII. Ecological Exposure Assessment

A. Ecological Data

In 1993 the Agency assessed the hazards posed to nontarget terrestrial and aquatic organisms resulting from their exposure to iron sulfates (USEPA 1993). Because information specific to iron citrate is not available, EPA is relying on the iron sulfate ecological hazard assessment (USEPA 1993) to describe ecological hazards resulting from exposure to iron. This is reasonable given that the concentration of iron citrate in the formulation will be low (1%) and the iron moiety of the sulfate salts and citrate is expected to behave in a similar fashion. Provided below is the summary and conclusion for the environmental fate assessment for the iron salts (USEPA 1993):

> No adverse effects to avian, mammalian or aquatic populations are anticipated from the use of iron salts. Iron is one of the most abundant elements and will be immobilized at the environmentally important pH range of 5-9. There is very little likelihood for runoff to aquatic systems since the parent compounds convert very rapidly to less soluble forms in the environment. Furthermore, these oxidized iron compounds bind tightly to soil under turf.

VIII. Risk Characterization

A. Human Health

The Shepherd Chemical Company is requesting that ferric citrate be exempt from the requirement of tolerance in or on raw agricultural commodities when used as an inert ingredient stabilizing agent in pesticide formulations under 40 CFR 180.910. In considering the potential risk posed by the use of ferric as an inert ingredient in a pesticide formulation, the Agency considered available toxicity and exposure information.

Ferric citrate is not acutely toxic via the oral route. In subchronic toxicity using mice, no effects were noted at the maximum tolerated dose, which is 0.12% ferric citrate in distilled water (this is approximately equivalent to 0.17 mg/kg/day). In chronic toxicity testing, no effects were seen at 0.22 mg/kg/day. Ferric citrate has not been shown to be mutagenic or carcinogenic. Finally, no developmental and reproductive effects have been shown. Based on this information there is no concern, at this time, for increased sensitivity to infants and children to ferric citrate when used as an inert ingredient in pesticide formulations. For the same reason, 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.

To characterize the chronic dietary risk resulting from the use of ferric citrate as an inert ingredient, EPA estimated dietary exposure (see Table 2) and compared it to a toxicity endpoint. In the Pesticide Program the "population adjusted dose (PAD)" is commonly used as the toxicity endpoint for dietary risk assessment. A "population adjusted dose" or "PAD" is a reference dose (RfD) that has been adjusted to take into account the FQPA (Food Quality Protection Act of 1996) Safety Factor. For ferric citrate, EPA is using the "Tolerable Upper Intake Level" (UL) as the toxicity endpoint for risk characterization. Because the NAS DRIs, which include UL, have been so extensively peer-reviewed, are so widely accepted, and were developed for dietary assessment purposes EPA believes that using these for its dietary risk assessment is appropriate.

The National Academy of Sciences IOM establishes DRIs which are "reference values that are estimates of nutrient intakes to be used for planning and assessing diets for apparently healthy people" (IOM 2001). DRI's include: RDA's and UL's. An RDA is "the dietary intake level that is sufficient to meet the nutrient requirement of nearly all (97 to 98 percent) of healthy individuals in a particular life stage and gender group." A UL is "the highest level of nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population. As intake increases above the UL, the risk of adverse effects increases." IOM (2001) has established UL's and RDA's for iron; they are provided in Tables 3 and 4, respectively. The critical adverse effect for the UL is GI distress with a LOAEL of 70 mg/day (IOM 2001).

Table 3. Tolerable Upper Intake Levels[1] for Iron in Terms of mg/kg bw/day

Age Group (years)	Iron Level (mg/kg bw/day)		
	Males and Females	During Pregnancy (females only)	During Lactation (females only)
0 to 3	3.3	NA	
4 to 8	1.8		
9 to 13	0.98		
14 to 18	0.74	0.79	0.79
19 to 50	0.63	0.69	0.69
51+	0.63	NA	

[1]UL's, as provided by IOM (2001) are reported in units of mg/day (for iron, the UL's range from 40 to 45 mg/day). EPA assumed that a child under 3 years of age weighs 12.2 kg; a 4 to 8 year-old weighs 22.8 kg; a 9 to 13 year-old weighs 41.0 kg; a 14 to 18 year-old weighs 60.6 kg; and an average adult weighs 71.8 kg. In addition, EPA assumes that a 14 to 18 year-old female weighs 56.9 kg and a 19 to 50 year-old female weighs 65.4 kg. (USEPA 1997)

Table 4. Recommended Dietary Allowances1 for Iron (mg/kg/day) in Terms of mg/kg bw/day

Age Group (years)	Iron Level			
	Males	Females	During Pregnancy (females only)	During Lactation (females only)
<1	1.21		NA	
1 to 3	0.53			
4 to 8	.44			
9 to13	0.20			
14 to18	0.18	0.26		0.18
19 to 50	0.11	0.28	0.41	0.14
51+	0.11		NA	

[1]RDA's, as provided by IOM (2001) are reported in units of mg/day (for iron, the UL's range from 7 to 27 mg/day. EPA assumed that a child less than one year weighs 9.1 kg; a 1 to 3 year-old weighs 13.3 kg; a 4 to 8 year-old weighs 22.8 kg; a 9 to 13 year-old weighs 41.0 kg; a 14 to 18 year-old weighs 60.6 kg; and an average adult weighs 71.8 kg. In addition, EPA assumes that a 14 to 18 year-old female weighs 56.9 kg and a 19 to 50 year-old female weighs 65.4 kg. (USEPA 1997)

Comparing estimated dietary exposure (see Table 2 for details of calculations) to the appropriate UL's (see Table 3), a metric of dietary risk is calculated; it is expressed as % of the UL. Provided in Table 5 is a summary of the estimated % of the UL.

Table 5. Estimated Chronic Dietary Risk for Ferric Citrate Use in Glyphosate (USEPA 2007)

Population Subgroup	Estimated Exposure to Ferric Citrate[2] (mg/kg/day)	UL's[3] (mg/kg/day)	Risk Metric (% of the UL)[3]	
			For Ferric Citrate	For Ferric Citrate as 1% in Formulation
U.S. Population (total)	0.120	0.63	19.0	0.19
All infants (<1 year)	0.245	3.3	7.4	0.07
Children (1-2 years)	0.422	3.3	12.8	0.13
Children (3-5 years)	0.310	1.8	17.2	0.17
Children (6-12 years)	0.174	1.8	9.7	0.10
Youth (13-19 years)	0.100	0.74	13.5	0.14
Adults (20-49 years)	0.087	0.63	13.8	0.14
Adults (50+ years)	0.086	0.63	13.7	0.14
Females (13-49 years)	0.087	0.63	13.8	0.14

[1]See Table 2 for calculations.
[2]The UL's are calculated in Table 3.
[3]Calculated by dividing the Adjusted Estimated Exposure by the UL and multiplying by 100.

As shown in Table 5, the '% of the UL' for the overall U.S. population is about 19%; the '% of the UL' for young children is about 7%. Please note that these estimates of dietary risk, which represent the contribution for food only, are very conservative. If 1% ferric citrate were used in the formulation, the '% of the UL' for the U.S. population would be less than 1% and the '% of the UL' for young children also less than 1%.

Looking at the other potential sources of iron exposure: on a daily basis average adults should consume 0.11 mg/kg/day (this is the RDA) of iron to maintain health (IOM 2001). Contrasting the amount that EPA expects an average adult to be exposed to through use of ferric citrate as an inert ingredient (0.0012 mg/kg/day), the pesticidal exposure is quite small. Regarding drinking water, iron is a naturally-occurring element ground and surface waters. Some exposure is expected but is not expected to be of concern to human health. EPA's Office of Ground Water and Drinking Water regulates iron as a secondary contaminant. Secondary contaminants are those that are considered to be "nuisance" chemicals (e.g., affect taste or color) rather than health concerns (USEPA 1992). EPA expects EPA expects that when used as an inert ingredient in pesticide products, ferric citrate would either remain on the plant or be washed off with rain or irrigation where it would be adsorbed to the soil. The Agency does not expect that it would deposit in ground or surface water. As a pharmaceutical, about a quarter of the U.S. population is estimated to ingest about 0.014 mg/kg/day of iron; again, compared to the RDA, this exposure is low. Therefore, dietary (food and drinking water) exposures of concern are not anticipated from use of ferric citrate in pesticides. Exposures from residential uses of pesticides containing ferric citrate, and from consumer products containing the chemical, are not expected to be of concern considering its low dermal and inhalation toxicity.

Taking into consideration all available information on ferric citrate, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to ferric citrate when used as an inert ingredient in pesticide formulations when considering dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, the exemption from the requirement of a tolerance requested by the petitioner, The Shepherd Chemical Company, for residues of ferric citrate, can be considered assessed as safe under section 408(q) of the FFDCA.

B. Ecological

Based on a previous Agency environment and ecological risk assessment for iron salts (USEPA 1993), EPA concludes that ferric citrate as an inert ingredient in pesticide formulations does not pose ecological risks of concern.

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