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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 6, 2005

ACTION MEMORANDUM

SUBJECT: Inert Ingredient Tolerance Reassessments – Cerous Chloride, Dysprosium Chloride, Europic Chloride, Lanthanum Chloride, Scandium Chloride, Ytterbium Chloride and Yttrium Chloride (CAS Reg. Nos. 7790-86-5, 10025-74-8, 10025-76-0, 10099-58-8, 10361-84-9, 10361-91-8 and 10361-92-9)

FROM: Dan Rosenblatt, Chief
Minor Use, Inerts, and Emergency Response Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

Action: Reassessment of seven (7) inert ingredient exemptions from the requirement of a tolerance. The tolerance exemptions are to be maintained. The spelling error for Cerous Chloride in 40 CFR § 180.920 will be corrected.

Chemicals: Cerous Chloride, Dysprosium Chloride, Europic Chloride, Lanthanum Chloride, Scandium Chloride, Ytterbium Chloride and Yttrium Chloride
CFR: 40 CFR § 180.920 [formerly 40 CFR § 180.1001(d)]
CAS #: CAS Reg. Nos. 7790-86-5, 10025-74-8, 10025-76-0, 10099-58-8, 10361-84-9, 10361-91-8 and 10361-92-9

Use Summary: The rare earth chlorides have a wide variety of scientific and industrial applications. They are used in superconductors, lasers, magnets, catalytic converters, fertilizers, super alloys, cigarette lighters and as catalysts in the production of petroleum and synthetic products. They are also used as pharmaceutical intermediates and as calcium probes in biochemical and physiological studies. The rare earth chlorides are used as inert tagging agents in agricultural herbicides and fungicides to distinguish one company's formulation from a competitor's.

List Reclassification Determination: The rare earth chlorides are classified as a List 3 inert ingredient. Based on the reasonable certainty of no harm safety finding and the existing 40 CFR §180.920 use limitation, the rare earth chlorides are reclassified as List 4B ingredients.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the seven (7) exemptions from the requirement of a tolerance for the inert ingredients, cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride, and with the List determination, as described above. I consider the seven (7) exemptions from the requirement of a tolerance for the rare earth chlorides established in 40 CFR §180.920 [formerly 40 CFR§180.1001(d)] to be reassessed as of the date of my signature, below.

Lois A. Rossi

Lois A. Rossi, Director
Registration Division

Date: May 10, 2005

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

May 6, 2005

MEMORANDUM

SUBJECT: Reassessment of the Seven Exemptions from the Requirement of a Tolerance for Cerous Chloride, Dysprosium Chloride, Europic Chloride, Lanthanum Chloride, Scandium Chloride, Ytterbium Chloride and Yttrium Chloride

FROM: Tracy Ward, Biologist Tracy Ward 5/6/05
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

THROUGH: Pauline Wagner, Inerts Team Coordinator Pauline Wagner 5/6/05
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

TO: Dan Rosenblatt, Chief
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

Background

Attached is the science assessment for cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride, also know as some of the rare earth chlorides. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, and environmental fate and ecotoxicity of these chemical compounds. The purpose of this document is to reassess the seven exemptions from the requirement of a tolerance for residues of the rare earth chlorides as required under the Food Quality Protection Act (FQPA).

Executive Summary

This report evaluates cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride, pesticide inert ingredients for which seven exemptions from the requirement of a tolerance exist for their residues when used in pesticide formulations (at a 10 ppm limit, alone or in combination) applied to growing crops only under 40 CFR §180.920 [formerly 40 CFR §180.1001(d)] for use as tagging agents.

The rare earth chlorides are derived from rare earth elements that occur naturally in the earth's crust at estimated levels of 1 to 66 ppm. The rare earths elements are present in trace amounts in plants and animals and thus comprise typical dietary exposure. They have a wide variety of industrial applications (including use in fertilizers, superconductors, lasers and magnets) and are used in biochemical and physiological research. The rare earth chlorides are also used as inert ingredients in agricultural pesticide formulations as tagging agents, which distinguish one company's formulation from a competitor's.

Based on the available toxicity data, the rare earth chlorides appear to have moderate acute and chronic toxicity, but at higher concentrations than would be expected to occur from exposure resulting from pesticidal uses. The rare earth chlorides have high median lethal doses (LD_{50}). However, the substances cause severe eye irritation and severe irritation in abraded skin. They are poorly absorbed by the gastrointestinal tract and by unbroken skin, but slight liver damage has been demonstrated in a subchronic oral toxicity study at high doses. The literature indicates that chronic inhalation exposure to the rare earth chlorides may cause pneumoconiosis in humans. There are no indications of carcinogenicity in the rare earth chlorides. Mutagenicity studies on these substances have mixed results, but are predominately negative.

The rare earth chlorides evaluated here exhibit acute aquatic toxicity at concentrations greater than 100 ppm and chronic toxicity at concentrations persisting for more than 21 days at concentrations greater than 30 ppm based on structure activity relationships.

Very small quantities (10 ppm) of rare earth chlorides are used as tagging agents in herbicide and fungicide formulations, and therefore they are not expected to pose a hazard to humans or the environment. Although rare earth chlorides have been shown to exhibit some acute and subchronic toxic effects, the risk of exposure to these substances when used in very small amounts as inert ingredients in pesticides is well below naturally occurring levels of the substances in the environment.

Taking into consideration all available information on the rare earth chlorides it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to these chemicals 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 seven exemptions from the requirement of a tolerance established for residues of rare earth chlorides in/on raw agricultural commodities can be considered reassessed as safe under section 408(q) of the FFDCA.

I. Introduction

This report evaluates cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride, which for the purposes of this assessment are called rare earth chlorides. These chemicals are pesticide inert ingredients for which seven exemptions from the requirement of a tolerance exist for their residues when used in pesticide formulations applied to growing crops only under 40 CFR §180.920 [formerly 40 CFR §180.1001(d)]. The exact tolerance exemption expressions, CFR references, CAS numbers and use patterns are detailed in **Table 1** below.

The rare earth chlorides are derived from a group of chemically related elements called rare earths. These rare earth metals are part of a relatively abundant group of 17 elements found in many minerals. The rare earths are mined from minerals in oxide form and are then refined to produce rare earth chlorides and other compounds. Many of these minerals are complex silicates or phosphates and usually contain several of the rare earth elements. Monazite sand is the most important source of these minerals.

World reserves of rare earth metals are estimated by the U.S. Geological Survey at 100 million tons (Hedrick, 1997). The largest resource of rare earths is in China, and there are substantial deposits in the United States, Scandinavia, India, and the Soviet Union.

II. Use Information

Pesticides

The seven tolerance exemptions for the rare earth chlorides when used as inert tagging agents in agricultural herbicides and fungicides are listed below in **Table 1**.

Table 1. Tolerance Exemptions Being Reassessed in this Document

Tolerances Exemption Expression	CAS Reg. No.	40 CFR § [1]	Use Pattern (Pesticidal)	List Classification
Carous chloride[2]	7790-86-5	180.920	Tagging agent (10 ppm in formulation)	3
Dysprosium chloride	10025-74-8	180.920	Tagging agent (10 ppm in formulation)	3
Europic chloride	10025-76-0	180.920	Tagging agent (10 ppm in formulation)	3
Lanthanum chloride	10099-58-8	180.920	Tagging agent (10 ppm in formulation)	3
Scandium chloride	10361-84-9	180.920	Tagging agent (10 ppm in formulation)	3
Ytterbium chloride	10361-91-8	180.920	Tagging agent (10 ppm in formulation)	3
Yttrium chloride	10361-92-9	180.920	Tagging agent (10 ppm in formulation)	3

1. Residues listed in 40 CFR §180.920 [formerly 180.1001(d)] are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.
2. The current spelling of cerous chloride in 40 CFR §180.920 is incorrect. The spelling error will be corrected in a future Federal Register Notice.

Other Uses

Rare earth chlorides have a wide variety of scientific and industrial uses. They are used as catalysts in the production of petroleum and synthetic products. They are also used in catalytic converters, superconductors, alloys, fertilizers, abrasives, lasers, magnets, lamp and cathode-ray tube phosphors, oxygen sensors, structural ceramics, super alloys, motion picture projectors, X-ray intensifying screens, flints and cigarette lighters.

In addition to their industrial uses, the rare earth chlorides are reportedly used in the synthesis of pharmaceutical intermediates, in protecting teeth from cavities, as an effective antiseptic drug for gram-negative bacteria and fungi, and as Ca^{+2} probes in biochemical and physiological studies.

III. Physical and Chemical Properties

Some of the physical and chemical characteristics of cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride are found in Appendix A.

These seven rare earth metal chloride compounds are derived from a group of chemically related elements in Group IIIB, or the lanthanide series, of the periodic table. Because scandium and yttrium resemble the rare earths so closely, they are often included in studies of the rare earths.

The metals usually occur together in minerals as their oxides and are difficult to separate because of their physical/chemical similarity. They are typically silver, silvery-white, or grey. They are also relatively soft metals with a high luster, but tarnish quickly in the air. Some of their common chemical and physical properties include high melting and boiling points, high electrical conductivity, high reactivity, similar water solubility, and paramagnetic properties. They burn easily and tend to react with most nonmetals.

IV. Hazard Assessment

A. Hazard Profile

Limited information is available to address the toxicity of the rare earth chlorides, however, the available information is adequate for this assessment. Literature found using the National Library of Medicine's ToxNet at http://toxnet.nlm.nih.gov, was used to assess the toxicity of the rare earth chlorides.

The literature suggests that the toxicological effects from exposure to high concentrations of the rare earth chlorides are low, with the greatest concern being acute toxicity effects for eye irritation. The rare earth chlorides are not irritants to and are not absorbed by intact skin, and they are poorly absorbed from the gastrointestinal tract. However, there is concern for subchronic toxicological effects on the liver. There is a potential for respiratory disease from chronic inhalation exposure to rare earth chloride dusts. The rare earth chlorides appear not to be carcinogenic, but have mixed results on mutagenicity tests.

B. Toxicological Information

The rare earth chlorides are grouped together as lanthanides in the periodic table because they share similar chemical and physical properties, such as the high melting points and low water solubilities listed in **Appendix A**. Therefore, studies summarized below describing one or more rare earth chlorides are used in this assessment to characterize the chemicals as a group.

Haley, et al, studied the toxicology of rare earth chlorides (1965 and 1966) and summarized their findings in a review (1965). For acute toxicity, male CF1 mice were fed up to 1.0% of dysprosium, europium, scandium or ytterbium chloride mixed with their food. The median lethal doses (LD_{50}) were, respectively, 4,000, 5,000, 7,650, and 6,700 mg/kg of body weight. These are toxicity categories III and IV.

For each rare earth chloride, Haley, et al (1965 and 1966), conducted Draize tests for eye irritation in rabbits with a 0.1 mL of a 50% aqueous solution of the salt. The eye tests resulted in no detectable damage to the rabbits' corneas or irises, but moderate to severe conjunctivitis was observed which healed completely after 38 days. For the skin tests, 0.5 g of each salt was applied to rabbits' abraded skin, with severe irritation resulting. Healing of the skin occurred up to 45 days later, with scarring and some epilation. Haley, et al, noted that the rare earth salts had no effect on intact skin.

In a twelve week subchronic study (Haley, et al, 1965 and 1966), rats were fed up to 1% (10,000 ppm) of each of the four compounds in their diet. Yttrium chloride caused perinuclear vacuolization in the liver, but there were no other adverse effects noted. Haley, et al, suggested that lack of adverse effects indicated lack of absorption of significant quantities of the rare earth chlorides tested in the gastrointestinal tract.

A 1978 study by Stineman, et al, supported Haley's observation. Mice were fed cerium chloride at concentrations up to the LD_{25} (LD_{50}'s for other rare earth chlorides ranged from 4,000 to 7,650 mg/kg) to determine the tissue/organ distribution and observe behavioral changes. The researchers found that cerium was poorly absorbed in the gastrointestinal tract, resulting in no tissue level concentrations and no behavior alterations.

There are no available inhalation toxicity studies for rare earth chlorides. However, there were several reports of individuals with chronic occupational inhalation exposure to high concentrations of rare earth dusts who developed pulmonary fibrosis and pneumoconiosis (Sabbioni, et al (1982) and Haley (1991)). The rare earth chlorides are not volatile, so there is low concern for inhalation exposure to vapors.

In the Health Council of the Netherlands assessment in 2000, Ames mutagenicity tests for yttrium chloride, using *S. typhimurium* strains TA98, TA100, TA102, TA1537 and TA2637, were negative. The Council also noted that yttrium chloride did not induce micronuclei in mouse bone marrow *in vitro,* but did induce micronuclei and damage to DNA in human lymphocytes *in vitro.* This suggests the potential for genotoxicity in humans, however, no evidence of cancer has been reported in human populations as a result of exposure to the rare earth chlorides.

C. Special Considerations for Infants and Children

While rare earth chlorides have demonstrated acute and chronic toxic effects, they occurred at high concentrations (1% in diet, or 10,000 ppm). The Agency expects that any exposure to the rare earth chlorides, when used as inert ingredients in pesticide formulations, will occur at levels well below the natural availability of the lanthanide metals themselves in the environment, as well as in typical dietary exposures from plant and animal sources. For these reasons, a safety factor analysis has not been used to assess the risks resulting from the inert pesticidal use of the rare earth chlorides, and an additional tenfold safety factor for the protection of infants and children is unnecessary.

V. Environmental Fate Characterization/Drinking Water Considerations

Rare earth chlorides are very poorly soluble in water. Modeled water solubilities range from 10^{-2} to 10^{-5} mg/L. Rare earth chlorides are expected to strongly sorb to the soil. Inorganic materials such as the rare earths are not expected to volatilize. However, it is unlikely that these rare earth chlorides would add substantially to background contributions as a result of a pesticide product. Wang, et al's 2001 study supports this assessment.

Wang, et al (2001), measured quantities of soluble rare earths in rain water, surface runoff and soil water and found the concentrations to be, respectively, 0.69 μg/L, 5-7 μg/L, and 1-4 μg/L. Application of a rare earth mixture to soil did not change these concentrations. The authors suggested that it would require many applications over time before rare earths would accumulate significantly in the soil.

In a study conducted by Wen, et al (2001), fertilizer, containing rare earth chlorides as added ingredients, was applied to rice under field conditions. After application of 113 g/ha of lanthanum chloride and 209 g/ha of cerium chloride, there were no significant increases in soil concentrations of rare earths. In addition, only trace amounts (less than 1 μg/g of plant) of the rare earths were taken up by the rice. It was determined that plant roots accumulated the greatest proportion of rare earth elements, followed by stems, then leaves/grain.

In summary, application of fertilizers with high concentrations of rare earth chlorides appears not to substantially change the concentrations of rare earths in the soil, and only trace amounts of rare earths are taken up by plants. Very low concentrations of the rare earth chlorides are used as inert ingredients in pesticide formulations and they are not expected to increase levels in agricultural soils and drinking water above naturally present background levels.

VI. Exposure Assessment

The natural occurrence of rare earths in the lithosphere is well established at a concentration level of a few hundred ppm. They are therefore not "rare" metals, but are usually only found in very low concentrations in the presence of other rare earths. Cerium is the most abundant rare earth and is the 25th most abundant element of the 78 common elements with an estimated crustal abundance of 46-66 ppm. Yttrium is the second most abundant rare earth at an estimated 28.1-31 ppm. Scandium is the 31st most abundant element in the earth's crust at 5-25 ppm and is the lightest of the rare earth elements in terms of molecular weight. The estimated abundance in the earth's crust for the remaining rare earths being assessed in this review are as follows: dysprosium (4.5 ppm), europium (1.06-2.1 ppm), lanthanum (18-35 ppm), and ytterbium (2.66-3.1 ppm).

The general population is widely exposed to rare earths and their compounds in the earth's crust, and there are trace amounts of these substances in most plants and animals. Exposure to the rare earth chlorides occurs through the diet, through touching or handling of soil or products containing rare earths, and through inhalation of particulates in the air. These substances are used to make consumer and industrial products such as cigarette lighters, fertilizers, catalytic converters in automobiles, synthetic products and structural ceramics. Rare earths chlorides are also used in the making of pharmaceuticals and antiseptic drugs, and in biochemical and physiological research.

Exposure resulting from the use of the rare earth chlorides as tagging agents at less than 10 ppm (40 CFR §180.920) in pesticide products is anticipated to be much smaller than from the naturally occurring background level of exposure, and no further dermal, oral, or inhalation exposure estimation is necessary for this qualitative assessment. Dietary exposures of concern from food (crops and meats, including fish) and drinking water are not likely from the use of these chemicals in pesticide products.

VII. Aggregate Exposure

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

For cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the very small exposures resulting from their use as pesticide inert ingredients and the lack of human health concerns associated with exposure to the rare earth chlorides.

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."

EPA does not have, at this time, available data to determine whether the rare earth chlorides have a common mechanism of toxicity with other substances. 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 the rare earth chlorides and any other substances and these substances do not appear to produce toxic metabolites produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed the rare earth chlorides have 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.

VIX. Human Health Risk Characterization

Based on the information available from a variety of literature sources, the toxicity data for the rare earth chlorides is sufficient for a qualitative assessment. The rare earth chlorides are not irritants to and are not absorbed by intact skin, and they are poorly absorbed from the gastrointestinal tract. In high concentrations, they are severe eye irritants, and subchronic dietary exposure to rare earth chlorides may lead to liver damage. Inhalation exposure to high concentrations of the rare earth chloride dusts may lead to pulmonary fibrosis and pneumoconiosis. However, they are not volatile and little risk of inhalation exposure to vapors is expected. There are no indications of carcinogenicity in the rare earth chlorides. Mutagenicity studies on these substances have mixed results, but are predominately negative. There are no reports of cancer in humans caused by exposure to rare earth chlorides. Residues from the use of these substances as inert tagging agents in agricultural herbicides and fungicides are unlikely to exceed naturally occurring levels in the environment. Therefore, dietary exposures of concern from food (crops and meats, including fish) and drinking water are not likely from the use of these inert ingredients in pesticide products and they are not expected to pose a hazard to human health.

Taking into consideration all available information on cerous chloride, dysprosium chloride, europic chloride, lanthanum chloride, scandium chloride, ytterbium chloride and yttrium chloride, there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure 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 seven exemptions from the requirement of a tolerance established for residues of rare earth chlorides in or on raw agricultural commodities and animals can be considered reassessed as safe under section 408(q) of the FFDCA. The current spelling of cerous chloride in 40 CFR §180.920 is incorrect. The spelling error will be corrected in a future Federal Register Notice.

X. Ecotoxicity and Ecological Risk Characterization

The rare earth chlorides evaluated here exhibit acute aquatic toxicity at concentrations greater than 100 ppm and chronic toxicity at concentrations persisting for more than 21 days at concentrations greater than 30 ppm based on structure activity relationships. The results of the toxicity studies found in the Ecotox database reported slightly greater toxicity than predicted by the structure activity models. Nevertheless, when used as an inert ingredient in pesticide formulation s at 10 ppm (40 CRF §180.920), the amount of rare earth chlorides released to the environment is much smaller than existing levels in the earth's crust, waters, plants and animals. Adding high concentrations of rare earth chlorides do not add substantially to background contributions. Concentrations of the substances in the environment are well below toxicity thresholds. Therefore, use of these substances as pesticide inert ingredients is not expected to present a potential risk to nontarget aquatic or terrestrial species.

References:

EPA's Ecotox Database is available at (http://www.epa.gov/cgi-bin/ecotox_quick_search)

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Haley, T.J., et al. "Pharmacology and toxicity of europium chloride." *Journal of Pharmacological Sciences.* Vol. 54, (1965) pp. 643-645.

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Sabbioni, E., et al. "Long-term occupational risk of rare-earth pneumoconiosis: A case report as investigated by neutron activation analysis." *The Science of the Total Environment.* Vol. 26, Issue 1 (1982) pp. 19-32. (Abstract)

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Wen, B., et al. "The Influence of Rare Earth Element Fertilizer Application on the Distribution and Bioaccumulation of Rare Earth Elements in Plants under Field Conditions." *Chemical Speciation and Bioavailability*. Vol.13, Issue 2. (2001) pp.39-48.

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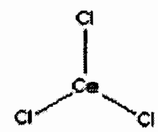
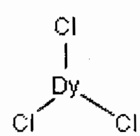
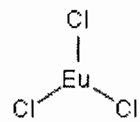
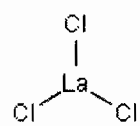
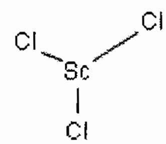
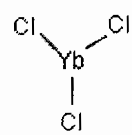
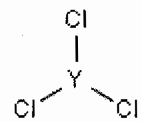
Appendix A

Physical and Chemical Properties of Seven Rare Earth Chlorides Measured (M) or Estimated (E)		
Parameter	**Value**	**Source**
Cerous Chloride (CAS Reg. No. 7790-86-5)		
Structure		ChemicalLand21.com, 2005
Molecular Weight	246.47	EPISuite, 2004
Water Solubility	2.057×10^{-4} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	882°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	1.067×10^{-16} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	6.77×10^{-20} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004
Dysprosium Chloride (CAS Reg. No. 10025-74-8)		
Structure		ChemIDplus, 2005
Molecular Weight	268.86	EPISuite, 2004
Water Solubility	1.377×10^{-2} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	680°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	1.823×10^{-15} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	7.13×10^{-17} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004

Physical and Chemical Properties of Seven Rare Earth Chlorides Measured (M) or Estimated (E)		
Parameter	**Value**	**Source**
Europic Chloride (CAS Reg. No. 10025-76-0)		
Structure		ChemIDplus, 2005
Molecular Weight	258.32	EPISuite, 2004
Water Solubility	3.898×10^{-4} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	850°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	1.814×10^{-16} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	2.08×10^{-19} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004
Lanthanum Chloride (CAS Reg. No. 10099-58-8)		
Structure		ChemIDplus, 2005
Molecular Weight	245.26	EPISuite, 2004
Water Solubility	3.291×10^{-4} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	860°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	1.432×10^{-16} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	1.46×10^{-19} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004

Physical and Chemical Properties of Seven Rare Earth Chlorides
Measured (M) or Estimated (E)

Parameter	Value	Source
Scandium Chloride (CAS Reg. No. 10361-84-9)		
Structure		ChemIDplus, 2005
Molecular Weight	151.32	EPISuite, 2004
Water Solubility	4.814×10^{-5} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	960°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	1.774×10^{-17} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	4.29×10^{-21} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004
Ytterbium Chloride (CAS Reg. No. 10361-91-8)		
Structure		ChemIDplus, 2005
Molecular Weight	279.40	EPISuite, 2004
Water Solubility	2.132×10^{-4} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	875°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	1.492×10^{-16} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	8.65×10^{-20} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004

Physical and Chemical Properties of Seven Rare Earth Chlorides Measured (M) or Estimated (E)		
Parameter	**Value**	**Source**
Yttrium Chloride (CAS Reg. No. 10361-92-9)		
Structure		ChemIDplus, 2005
Molecular Weight	195.26	EPISuite, 2004
Water Solubility	7.146×10^{-3} mg/L at 25° C (E)	EPISuite, 2004
Melting Point	721°C (M)	Sigma-Aldrich.com, 2005
Henry's Law Constant	6.4×10^{-16} atm-m3/mole @ 25°C (E)	EPISuite, 2004
Vapor Pressure	1.78×10^{-17} mmHg @ 25°C (E)	EPISuite, 2004
Octanol/Water Partition Coefficient	Log P = 1.16 (E)	EPISuite, 2004

Versar inc.

MEMORANDUM

TO:	Kathryn Boyle	cc:	Chuck Peck 10.4700.4950.001
FROM:	Laura Guziak/Kathy Coon/Jim Buchert		
DATE:	January 28, 2005		
SUBJECT:	Draft Science Assessment for the Rare Earth Metal Chlorides		

Attached is the Draft Science Assessment for the Rare Earth Metal Chlorides. The assessment evaluates human health toxicity data to reassess the existing tolerance exemptions for the Rare Earth Metal Chlorides. The assessment was prepared based on information and the template provided by OPP/OREB. Additional references obtained by Versar were also used in the preparation of the assessment. Please note that a reference on the human health risk from cerium was recently located by Versar and might be of interest (www.healtheffects.org/Pu.PDF). Areas of uncertainty have been highlighted.

Please give us a call if you have any questions.

Lower Risk Pesticide Chemical Focus Group

Draft Science Assessment for the Rare Earth Metal Chlorides

I. Executive Summary

This review is being conducted to reassess the existing inert ingredient tolerance exemptions for the seven Rare Earth Metal Chlorides as described below:

- Cerous chloride ($CeCl_3$, CAS Reg. No. 7790-86-5)
- Dysprosium chloride ($DyCl_3$, CAS Reg. No. 10025-74-8)
- Europic chloride ($EuCl_3$, CAS Reg. No. 10025-76-0)
- Lanthanum chloride ($LaCl_3$, CAS Reg. No. 10099-58-8)
- Scandium chloride ($ScCl_3$, CAS Reg. No. 10361-84-9)
- Ytterbium chloride ($YbCl_3$, CAS Reg. No. 10361-91-8)
- Yttrium chloride (YCl_3, CAS Reg No. 10025-94-2)

The rare earths are a relatively abundant group of 17 elements consisting of scandium, yttrium, and the lanthanides. They are found in many minerals. Many of these minerals are complex silicates or phosphates and usually contain several of the rare earth elements. Monazite sand is the most important source of these minerals. The rare earth elements are metallic in character and all form oxides which are refined to produce rare-earth chlorides, nitrates, and other concentrates and compounds. The rare earths are physically hard to separate, share similar chemical properties, and are used in a wide variety of applications. Consumer exposure to the rare earths is limited.

Limited information is available to address the toxicity of the rare earth chlorides, however, the available information suggests that the toxicological effects from exposure to the rare earth chlorides appear slight, with the greatest concern being acute toxicity effects for eye and skin irritation. There is conflicting evidence on potential negative effects on growth and exposure via inhalation. However, the rare earth metals are neither carcinogenic nor mutagenic. The Agency is conducting a qualitative assessment.

II. Background

The tolerance exemptions for the seven rare earth metal chlorides were established in 1996 in response to pesticide/petition ___, as requested by ___. The original documentation indicated that the decision to establish the tolerance exemptions rested almost solely on the small exposure. There was no discussion on toxicity. The data submitted in support of the petition included only basic information on the rare earth metals and of their occurrence in plants.

The tolerance exemptions being reassessed in this document, the 40 CFR citation of the established tolerance exemptions, and the use pattern as an inert ingredient are listed below in Table 1.

Table 1. Tolerance Exemptions Being Reassessed in this Document

Tolerances Exemption Expression	40 CFR ◊	Uses
Cerous chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
Dysprosium chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
Europic chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
Lanthanum chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
Scandium chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
Ytterbium chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
Yttrium chloride	180.920 [formerly 180.1001(d)]	Tagging agent (10 ppm in formulation)
◊Residues listed in 40 CFR 180.920 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.		

The tolerance exemptions were established based solely on the low potential for human exposure to the rare earth metal chlorides when used as tagging agents. Tagging agents are marker or tracer elements that are used for the purposes of detection or identification. There is a limitation expressed in the exemptions of 10 ppm in the formulation.

Rare earth compounds have a wide variety of scientific and industrial uses. They are used as catalysts in the production of petroleum and synthetic products. They are also used in superconductors, alloys, fertilizers, abrasives, lasers, magnets, lamp and cathode-ray tube phosphors, oxygen sensors, structural ceramics, superalloys, motion picture projectors, X-ray intensifying screens, flints, cigarette lighters, and in the synthesis of pharmaceutical intermediates. In addition to their industrial uses, the rare earths are reportedly effective as an antiseptic drug for gram-negative bacteria and fungi, and in protecting teeth from cavities, and are used as Ca^{+2} probes in biochemical and physiological studies.

Levels in Pharmaceuticals?

III. Description of the Rare Earth Metals

The rare earths are a group of 15 chemically related elements in the Group IIIB of the Periodic Table (lanthanide series). They include elements of atomic numbers 57 to 71 inclusive: lanthanun (La), cerium (Ce), prasedymium (Pr), neodymium (Nd), promethium (Pm), samarium (Sm), europium (Eu), gadolinium (Gd), terbium (Tb), dysprosium (Dy), holmium (Ho), erbium (Er), thulium (Tm), ytterbium (Yb), and lutetium (Lu). Because scandium (Sc-atomic number 21) and yttrium (Y-atomic number 39) resemble the rare earths so closely, they are often included in studies of the rare earths.

The metals usually occur together in minerals as their oxides and are difficult to separate because of their physical/chemical similarity. They are typically silver, silvery-white, or grey. They are also relatively soft metals with a high luster, but tarnish quickly in the air. Some of their common chemical and physical properties include high melting and boiling points, high electrical conductivity, high reactivity, similar water solubility, and paramagnetic properties. They burn easily and tend to react with most nonmetals.

IV. Occurrence in the Earth's Crust

The natural occurrence of rare earths in the lithosphere is well established at a concentration level of a few hundred ppm. They are therefore not "rare"metals but are usually only found in very low concentrations in the company of other rare earths. Cerium is the 25th most abundant element of the 78 common elements with an estimated crustal abundance of 46-66 ppm. Yttrium is the second most abundant rare earth at an estimated 28.1-31 ppm. Scandium is the 31st most abundant element in the earth's crust at 5-25 ppm and is the lightest of the rare earth elements. The estimated abundance in the earth's crust for the remaining rare earths being assessed in this review are as follows: dysprosium (4.5 ppm), europium (1.06-2.1 ppm), lanthanum (18-35 ppm), and ytterbium (2.66-3.1 ppm).

The rare earths naturally occur together in minerals as their oxides. They are found with other nonmetals in the 3+ oxidation state. World reserves of rare earths are estimated by the U.S. Geological Survey at 100 million tons (1997). The largest resource of rare earths is in China. There are also substantial deposits in the United States, Scandinavia, India, and the Soviet Union. In 1996, 20,400 tons of rare earth oxide were mined in the United States. These deposits are composed of many minerals, the most important of which is monazite, a heavy dark sand of variable composition. The only rare earth being assessed in this document for which there are not rich resources is scandium.

V. Toxicity Reviews and Assessments

Three published studies are used to assess the toxicity of the rare earths to human health. Information for the studies was originally obtained from the National Library of Medicine's database TOXLINE Special. TOXLINE Special is available on the TOXNET system at http://toxnet.nlm.nih.gov and provides bibliographic information, most with abstracts and/or indexing terms, from an assortment of specialized journals, technical reports, and research projects. Complete articles were obtained for this review, if available.

Studies of Nutritional Safety on Some Heavy Metals in Mice

In 1975, the Journal of Nutrition published a study by Hutcheson et al. on the safety of using heavy metals as nutritional markers. The following abstract was obtained directly from TOXLINE Special.

> "Heavy metals were proposed as nutrient markers to allow the accurate determinations of the time of passage, nutrient intake or apparent utilization of multiple nutrients. In order to evaluate possible toxic effects of Sc, Cr, La, Sm, Eu, Dy, Tb, Tm and Yb oxides, and BaSO4 on growth, general development, reproduction and lactation, mice were fed different levels of these compounds for 3 generations. The amounts of elements fed were 0, 1, 10, 100 and 1000 times the use amount. The use amounts were (in ppm): Sc, 0.12; Cr, 0.02; La, 0.40; Sm, 0.80; Eu, 0.036; Tb, 1.20; Dy, 1.20; Tm, 0.08; Yb, 0.12; and Ba, 0.008. The use amount was 1/5 of the concentration required for activation analysis. Mortality and morbidity were negligible. No consistent growth rate changes were observed; different groups showed different growth rates during different generations. The number of mice born showed no significant differences among treatment groups. Survival, growth rate, hematology, morphological development, maturation, reproduction and lactational performance were comparable in mice fed the different levels of 10 heavy metal oxides to those mice fed the basal diet."

The authors concluded that the heavy metal compounds tested, including Sc, La, Eu, Dy, and Yb, could safely be used as nutritional markers. When these same diets and markers were fed to monkeys for 8 weeks at 10 times the use level, no tissues were found with any of the metals present above the analytical detection limit. A review of the literature indicated no toxicity from oral intake of the heavy metals studied.

In addition, Hutcheson et al. noted the results of two earlier studies. A 1971 study showed that 5 ppm of scandium, added in drinking water, resulted in "a slight but significant suppression of growth of mice at different intervals of age during the first 6 months but not at later intervals..." A study conducted in 1965 concluded that "chronic ingestion of terbium, thulium, and ytterbium chlorides (1,000 and 10,000 ppm in the diet) caused some suppression of growth in rats; but dysprosium and other rare earth metal chlorides did not."

Exposure, Metabolism, and Toxicity of Rare Earths and Related Compounds

In 1996, the Environmental Health Perspectives Journal published an article by Hirano and Suzuki that presented an overview of the metabolism and health hazards of the 15 rare earths and related compounds, including the authors recent studies. The following information was extracted directly from the journal article.

Chemical Properties/Toxicity

> "The nitrates, chlorides, and sulfates of RE [rare earths] are soluble and their carbonates, phosphates, and hydroxides are insoluble...The differences in solubility among these ionic forms of RE seem to determine the metabolic fate of RE in the biological system. In general, the toxicity of lanthanoids decreases as the atomic number increases, probably due to greater solubility and ionic stability of heavier lanthanoids..."

Mortality

> "Mortality studies reveal that RE [rare earths] are not highly toxic (LD_{50} values for iv-injected RE are 10 to 100 mg/kg/bw and those of ip-injected RE are 150 to 700 mg/kg/bw); cytotoxicity of RE to macrophages is comparable to that of Cd or silica *in vitro*. These discrepancies in lethal toxicity between *in vivo* and *in vitro* studies seem to be due to chemical forms of RE in the experimental system because those cytotoxicity studies were carried out in culture medium without serum. It is of interest to study the toxicity of RE using macrophages and other cells in various culture conditions."

Effects on Lungs

> "...chronic exposure to RE [rare earth] dust probably causes pneumonoconiosis in humans...It has been shown that intratracheal instillation of YCI_3 caused granulomatous changes in the rat lung...Inhalational exposure to high concentrations of Gd_2O_3...and intratracheal instillation of YCl_3..., $LaCl_3$..., and $GdCl_3$ have been shown to cause pneumonitis and acute inflammation in the lung, e.g., infiltration of neutrophils and leakage of enzymes and proteins into the alveolar space, in mice and rats. The acute toxicity of YCl_3 in the rat lung was between those of ZnO and Cd compounds, judging from dose-related changes in lactate dehydrogenase activity in the bronchoalveolar lavage fluid..."

Effects on the Liver

> "Intravenously injected RE [rare earth] chlorides increase vascular permeability for low molecular weight substances...and cause necrosis in the liver...Hepatic endoplasmic reticulum (ER) has been shown to be the primary target of iv-injected $CeCl_3$ in the rat liver, and dilation, disorganization, and degranulation of rough ER and proliferation of smooth ER occurred following the iv injection ...suggesting that the liver is the primary target organ of iv-injected $CeCl_3$"

"It has been shown that iv injection of $CeCl_3$ caused fatty liver in female rats...but not in male rats...Intravenous injection of YCl_3, $TbCl_3$, $HoCl_3$ and $YbCl_3$ caused focal necrosis with Ca deposition in rats but $CeCl_3$ did not...patchy Ca deposition occurred in the focal necrotic area of the rat liver following iv injection of YCl_3 (~50 μg Y/g liver)...However, the reason that fatty liver was limited to female rats that received $CeCl_3$ remained unknown. It seems that iv injection of $CeCl_3$ produces lipid droplets in the liver of male mice..."

"There is a battery of reports about hepatic biochemical changes following iv injection of ionic RE [rare earths]...biochemical changes are consistent among RE; those biochemical changes are increase in triglyceride in the liver...and increases in leakage of hepatic enzymes into blood...RE-induced hepatic injury seems to reduce P450 content and P450-related enzyme activities in rat..and mouse... however, the decreases in P450 activities (coumarin 7-hydroxylase and 7-ethoxyresorufin *O*-deethylase) at 3 to 4 days after iv injection of $CeCl_3$ were preceded by increases in these enzyme activities at 1 to 2 days postinjection in DBA/2 mice...It has also been reported that ip injection of $CeCl_3$ causes lipid peroxidation and a decrease in gluthathione reductase activity in the chick liver..."

Table 2. Hepatic and Liver-associated Biochemical Changes Following Intravenous Injection of Rare Earths

Effect	RE compound	Animal	Dose
s-GOT, s-GPT↑	$CeCl_3$, $Ce(NO_3)_3$, $La(NO_3)_3$, YCl_3	Rat	2-10 mg Ce/kg,3-10 mg La/kg, 1 mg Y/rat
s-OCT↑	$CeCl_3$, $PrCl_3$, $LaCl_3$ YCl_3, $TbCl_3$, $HoCl_3$, $YbCl_3$	Rat	1.5-3 mg Ce/kg, 3 mg Pr/kg, 0.75 mg La/kg 9 mg Y/kg, 35 mg Tb/kg, 40 mg Ho/kg, 60 mg Yb/kg
Triglyceride (liver)↑	$CeCl_3$	Rat	10 mg $CeCl_3$/kg
ATP↓	$CeCl_3$	Rat	10 mg $CeCl_3$/kg
LPO↑	$LaCl_3$	Chick (ip)	250 mg $LaCl_3$/kg
GR↓	$LaCl_3$	Chick (ip)	250 mg $LaCl_3$/kg
COH, EROD, Cyp2a-4/5-m RNA↑↓	$CeCl_3$	Mouse	2 mg $CeCl_3$/kg, 0.5-2 mg Ce/kg

Effects on the Kidney, Spleen and Gastrointestinal Tract

"Ethoxyresorufin *O*-deethylase activity in the kidney was decreased following iv injection of $CeCl_3$ in mice...Lipid peroxidation was increased and glutathione content and antioxidant enzymes were decreased in the renal cortex following ip injection of $LaCl_3$ in chicks... Intravenous injection of $LaCl_3$ or $CeCl_3$ increased vascular permeability of the spleen in mice..., and both sc and po administration of Ce^{3+}-citrate caused hypertrophy, reticuloendothelial hyperplasia, and hyperactive lymphoid follicles in mice...Significant Ca deposition occurred in the spleen following ip injection of YCl_3...Oral administration of Ce^{3+}-citrate has been shown to cause focal hemorrhage, necrosis of mucosa, and neutrophil infiltration in the stomach and duodenum..."

Effects on the Eye and Skin

"Exposure to $EuCl_3$, $DyCl_3$, $HoCl_3$, and $ErCl_3$ caused conjunctivitis in rabbits when these RE [rare earth] chlorides were applied directly to their eyes...These RE chlorides have also been demonstrated to cause severe irritation when they are applied to abraded skin in rabbits and cause epilation and nodule formation when injected intradermally in guinea pigs...It has also been shown that sc injection of RE chlorides caused local calcification with mild fibrosis and accumulation of multinucleated giant cells, and the calcification area was increased with dose (up to 2 mg of RE chlorides) in mice..."

Effects on the Blood, Bone Marrow, and Other Cells/Tissues

"Intraperitoneal injection of $LaCl_3$ or $NdCl_3$ significantly decreased the contents of sulfhydryl groups, cholesterol, phospholipid and lipid peroxides, and activities of galactosidase, glucuronidase, acetylcholinesterase, NADH dehydrogenase, ATPase, and p-nitrophenyl phosphatase in the red blood cell membrane in chicks...It has also been shown that ip injection of $LaCl_3$ decreased contents of sulfhydryl groups and lipid peroxides and increased activities of glutathione peroxidase, glutahione reductase, glutanthione-S-transferase, and catalase in the bone marrow of chicks..."

"...ip injection of $LaCl_3$ caused a marked depression in the activities of neural Ca^{2+}-ATPase, Mg^{2+}-ATPase, and cholinesterase in chicks. The depression of these enzyme activities may be related to inhibitory effects of La^{3+} on binding of Ca^{2+} to brain synaptosomal membrane."

"The median lethal concentration (LC_{50}) for rat alveolar macrophages of CdO, $CdCl_2$, $LaCl_3$, $CeCl_3$, and Nd_2O_3 were 15, 28, 52, 29, and 101 μM, respectively, *in vitro*, and although La_2O_3 and Ce_2O_3 were less toxic than $LaCl_3$ and $CeCl_3$, respectively, Nd_2O_3 was more toxic than $NdCl_3$..."

Effects on Behavior, Pregnancy, and Offspring

"It has also been shown that ip injection of $LaCl_3$ (44 mg La/kg bw) increased the cessation of pregnancy and decreased the average litter size in pregnant mice...No malformation was observed in fetuses, even when the dams were administered po with a high dose of $RE(NO_3)_3$ (331 mg/$RE(NO_3)_3$/kg bw) starting from the 16^{th} day of gestation in rats"

Effects on Growth, Longevity, and Carcinogenicity

> "The aortic contents of cholesterol, collagen, elastin, and Ca and urinary hydroxyproline excretion were increased in rabbits when they were kept on an atherogenic diet; intake of La (40 mg $LaCl_3$/kg bw/day) significantly reduced the increases of these atherosclerotic parameters...The growth of mice was depressed when they were given 5 ppm of Sc^{3+} or Y^{3+} in drinking water, and the longevity was increased in Y^{3+}-fed mice...However, no effect on growth was found in rats that had been fed a diet containing 0.1 to 1% of $DyCl_3$, $HoCl_3$, or $ErCl_3$ for 12 weeks..."

> "No carcinogenicity of RE [rare earths] has been found in animals...In addition, at 0.5 to 50 mg/ml of $RE(NO_3)_3$ (a mixture of Ce, La, Nd, Pr, and Sm), Ames mutagenicity tests were negative..."

Hirano and Suzuki summarized that the deposition and retention of rare earth compounds following iv, po, se, intratracheal and inhalation exposure is determined by the chemical form of the rare earth. Chelated rare earths are excreted rapidly from the body via urine, whereas, unchelated ionic forms of rare earths form colloids in the blood and are deposited in the liver and spleen. Bone is also one of the target organs of the rare earths and clearance of the rare earths from bone is very slow. In addition, inhalational and intratracheal exposure to rare earths causes acute pneumonitis in animals. Long-term exposure to rare earth dusts appears to cause pneumonconiosis in humans. Mortality studies indicate that rare earths are not highly toxic. The authors recommend that more extensive studies, including those involving chronic exposure, be conducted.

Health-based Reassessment of Occupational Exposure Limits of Yttrium and Yttrium Compounds

The Health Council of the Netherlands reassessed the health-based occupational exposure limit for yttrium and yttrium compounds in 2000. In their reassessment, they noted that the "toxicity of yttrium is rather aspecific." Based on available data, the target organ for toxicity after exposure appears to be the lungs. In addition, "after lifetime dosing of mice via the drinking water, no carcinogenic or toxic effects were observed." Some yttrium compounds were also found to be irritating to the skin and eyes. It was expected that the differences in toxic effects of the various compounds was due to the differences in water-solubility. Because of the limited toxicological data base on yttrium and yttrium compounds, the Council could not recommend a health-based occupational exposure limit.

VI. Exposure to Rare Earth Metals

Consumer exposure to the rare earths is expected to be minimal. One route of potential exposure is through plants. Plants may absorb rare earths via their use in fertilizers or presence in soil.

A thesis prepared in 1975, by a student at the Helsinki University of Technology, examined the occurrence of rare earths in plants (Yliruokamen, 1975). Yliruokamen found that, in general, the mobility of the rare earth metal chlorides is low and they are not translocated from roots to the other parts of plants. Therefore, plants tend to have a low content of rare earths. Their content of rare earths is correlated with the rare earth content of the soils and rocks. In addition, studies have demonstrated that rare earths are among the elements strongly excluded by crop plants, with the relative concentration factor being < 0.01 (ppm in dry plant soil/ppm in dry soil). Increased uptake has been noted when chelating agents are involved but otherwise has only been documented in exceptional cases.

Various levels of rare earths in plants were reported by Yliruokamen following a literature review. One terrestrial plant known to accumulate high contents of rare earths in its leaves is the hickory tree. Concentrations of 2 to 2296 ppm of rare earths (as oxides) in dry matter were found by a researcher in 1938. Levels in other parts of the hickory tree were 140 ppm in the bark of taproot and 5 to 17 ppm in nuts.

In crop plants, the highest levels of rare earths (100-122 ppm) were found in corn leaves, and in rhubarb stalks and leaves. The lowest levels were found in tomato fruit and corn grain. Corn leaves and spinach, grown on substrates treated with gadolinite, contained 690 ppm and 168 ppm of rare earths, respectively. Both lanthanum and cerium have been detected in leguminous plants. Low levels of scandium and lanthanum have been found in tobacco, with higher levels found in the leaves than the stalks. In addition, it appears that the level of rare earths in plants increases during the growth period.

In addition to crop plants, the rare earths were also found in herbal plants used in homoeopathic medicines. Yttrium (2.5 - 30 ppm), cerium (300 - 1000 ppm), and ytterbium (1 - 30 ppm) were found in *Labiatae*. Both yttrium and ytterbium were found at 30 ppm in *Betonica brachyndota*.

The use of rare earth metals in fertilizers is based on early reports demonstrating that they stimulate plant growth. Widespread application of fertilizers containing rare earths has occurred in China. In a study in which fertilizer containing rare earth elements was applied to wheat, rice, and vegetables under field conditions, rare earth elements accumulated to different degrees in different parts of the plants (Bei Wen, et. al., 2001). The roots accumulated the greatest proportion of rare earth elements and the grains accumulated the least. Although no significant accumulation was observed in cereal grains, the study did not recommend the use of rare earth elements in fertilizers as a significant accumulation of rare earth elements was found in the edible parts of vegetables. However, at the same time, plants are believed to contain low levels of rare earth elements and therefore act as an efficient barrier against the transfer of rare earth elements from soil to animals and human beings through the food chain.

VII. Hazard Characterization

The toxicity of the rare earth metal chlorides is defined by the reviewed studies. Based on the limited data available, the toxicity of the rare earth chlorides appears to be low. Because the chlorides of the rare earths are soluble, they are excreted more rapidly from the body than the relatively insoluble rare earth compounds (hydroxides and oxides). In general the toxicity of the rare earths decreases as the atomic number increases due to greater solubility and ionic stability of the heavier rare earths. No chronic toxicity endpoints are available.

The available information suggests that the greatest concern from exposure to the rare earth metal chlorides are for eye and skin irritation. The lungs, liver, and bone are expected to be likely target organs from exposure to rare earths. However, since the nuclear era, Cerium^{144} has been detected in animal bones without any correlating adverse effects. Rare earths do not appear to be mutagenic or carcinogenic. One study suggests that they would be safe for use as nutritional multiple markers.

Consumer exposure to the rare earth metal chlorides is expected to be minimal with fertilizers and pharmaceutical preparations being the only consumer products through which direct exposure is possible. Consumers may also be exposed through crop plants because plants may absorb rare earth elements via their use in fertilizers or in the soil. However, studies have shown that rare earths are among the elements strongly excluded by crop plants.

VIII. Special Considerations for Infants and Children

Based on very limited developmental studies in laboratory animals, there is a potential concern for growth retardation in infants and children. However, additional studies are needed to evaluate the conflicting evidence of a concern. A safety factor analysis has not been used to assess risk. For the same reasons, the additional tenfold safety factor is unnecessary.

IX. 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." If chemicals are structurally related and all are low toxicity chemicals, then the risks either separately or combined should be low.

EPA does not have, at this time, available data to determine whether the Rare Earth Metal Chlorides have a common mechanism of toxicity with other substances. 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 the rare earth metal chlorides and any other substances and the rare earth metal chlorides do not appear to produce toxic metabolites produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed the rare earth metal chlorides have 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.

X. Conclusions

The Agency believes these chemicals to be of lower toxicity. There is no reason to expect that the reasonably forseeable uses of the rare earth metal chlorides will constitute any significant hazard. Even considering the potential for aggregate exposures, the use of Cerous chloride ($CeCl_3$, CAS Reg. No. 7790-86-5), Dysprosium chloride ($DyCl_3$, CAS Reg. No. 10025-74-8), Europic chloride ($EuCl_3$, CAS Reg. No. 10025-76-0), Lanthanum chloride ($LaCl_3$, CAS Reg. No. 10099-58-8), Scandium chloride ($ScCl_3$, CAS Reg. No. 10361-84-9), Ytterbium chloride ($YbCl_3$, CAS Reg. No. 10361-91-8), and Yttrium chloride (YCl_3, CAS Reg No. 10025-94-2) in a pesticide product should result in human exposure far below any dose level that could possibly produce an adverse effect.

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