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A Review of the Literature on the Toxicity of Rare-Earth Metals as it Pertains to the Engineering Demonstration System Surrogate Testing

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Contents

Summary

A review of data on animal and damaging human exposure to the rare-earth elements has been made. Incidental oral ingestion is considered to be harmless and accidental nonrespiratory uptake does not represent a health risk. Equipment design and operating procedures mitigate against dermatologic or ophthalmologic risk to workers and the public. Animal and human inhalation studies confirm the use of the Threshold Limit Value–Time Weighted Average (TLV–TWA) for yttrium as a conservative measure for evaluation of the Engineering Demonstration System (EDS) emissions of the lanthanons. This value (1 mg/m^3) is also consistent with the OSHA-established permissible exposure limit (PEL). Environmental exposures that are maintained at a level below the TLV/PEL value should result in no health impact to workers, visitors, or the public.

1. Introduction

Considerable data on the toxicology of the rare-earth metals and their compounds via oral ingestion or injection have been collected from animal studies at relatively high exposure levels. Data in the literature on inhalation, particularly of the oxides, and for damaging exposure of humans are less complete because human exposures have rarely reached toxic levels, not withstanding their widespread use. However, they do provide a basis for evaluating the health and environmental impact resulting from use of these materials.

This report:

- Provides a general introduction to the rare-earth elements.
- Reviews data on the toxicity of the rare earths from animal studies and the relatively rare occurrences of harmful human exposure.
- Discusses precautions for worker protection that should be taken with use of these materials.
- Relates scientific data with EDS operations.

Topics to be covered include:

— Definition of the term "rare-earth" elements.
— Geological occurrence.
— General physical and chemical characteristics.
— Uses and industrial exposure.
— Nonrespiratory studies.
  - Animals.
  - Humans.
— Inhalation studies.
  - Animals.
  - Humans.
— Dermatologic and ophthalmologic toxicity.
— Occupational exposure guidance and worker protection.

2. Definition of the Term Rare Earths

Although the rare-earth elements are not particularly rare, the term persists and refers to the elements in the lanthanide series (atomic numbers 57–71) plus yttrium (39). The use of the rare-earth elements in the Engineering Demonstration System (EDS) tests is limited to those in the lanthanide series that have no significant level of radioactivity. Thus, samarium, promethium, and lutetium are not considered and this report will deal only with chemical toxicity and ignore radiation issues. Since pure metals are used in the Program, the toxicology evaluation is focused on metals and metal oxides that would be the primary potential exposures in an occupational environment or accident.

The rare earths, their symbols, and their atomic numbers, which are pertinent to EDS tests, are shown in Table 1.

Table 1. Rare-earth elements pertinent to EDS tests and yttrium (Considine, 1984).

Name	Chemical symbol	Atomic No.
Yttrium	Y	39
Lanthanum	La	57
Cerium	Ce	58
Praseodymium	Pr	59
Neodymium	Nd	60
Europium	Eu	63
Gadolinium	Gd	64
Terbium	Tb	65
Dysprosium	Dy	66
Holmium	Ho	67
Erbium	Er	68
Thulium	Tm	69
Ytterbium	Yb	70

3. Geological Occurrence

The occurrence of many of the rare-earth elements in the earth's crust exceeds that of some commonly used industrial elements. Thus, for example, yttrium, cerium, lanthanum, and neodymium are present in greater quantities in the earth's crust than lead. Table 2 summarizes the natural occurrence of rare earths compared to some other important industrial metals.

Table 2. Natural occurrence of rare earths and other elements (Considine, 1984).

Rare earths	ppm	Other	ppm
Thulium	0.5	Gold	0.015
Terbium	0.9	Silver	0.1
Europium	1.2	Mercury	1.0
Holmium	1.2	Lead	16
Erbium	2.8	Cobalt	23
Dysprosium	3.0	Tin	40
Ytterbium	3.0	Bromine	50
Gadolinium	5.4	Nickel	80
Neodymium	28	Copper	100
Lanthanum	30	Zinc	130
Yttrium	33		
Cerium	60		

4. General Physical and Chemical Characteristics

All the rare-earth elements possess similar physical and chemical properties and it has historically been very difficult to separate them. Their common properties are associated with their particular atomic structure. Each has two outer electrons and eight or nine in the next inner shell. The electron structure varies in the third shell from the outside as shown in Table 3. The addition of electrons to the inner shells makes little change in many of their physical and chemical properties. All of the rare-earth metals are relatively soft, malleable, and have a bright silver luster. If finely divided, the metal powders will oxidize relatively quickly when exposed to air. When present in solid lumps, the metal will not undergo spontaneous combustion, but will oxidize slowly, comparable to the rusting of other metals. Because of similarities in their chemistry and toxicity, many authors discuss the characteristics of the rare-earth elements as a group. Within this group, however, there are differences between the toxicity of the individual rare-earth elements and their compounds (Stokinger, 1981; CRC, 1988). These differences are discussed later.

Table 3. Electron configuration of yttrium and the lanthanide series (CRC, 1988).

		Electron configuration					
		K	L	M	N	O	P
		1	2	3	4	5	6
Atomic No.	Element	s	s p	s p d	s p d f	s p d f	s p d f
39	Y	2	2 6	2 6 10	2 6 1	2	2
57	La	2	2 6	2 6 10	2 6 10 ..	2 6 1 ..	2
58	Ce	2	2 6	2 6 10	2 6 10 2	2 6	2
59	Pr	2	2 6	2 6 10	2 6 10 3	2 6	2
60	Nd	2	2 6	2 6 10	2 6 10 4	2 6	2
63	Eu	2	2 6	2 6 10	2 6 10 7	2 6	2
64	Gd	2	2 6	2 6 10	2 6 10 7	2 6 1 ..	2
65	Tb	2	2 6	2 6 10	2 6 10 9	2 6	2
66	Dy	2	2 6	2 6 10	2 6 10 10	2 6	2
67	Ho	2	2 6	2 6 10	2 6 10 11	2 6	2
68	Er	2	2 6	2 6 10	2 6 10 12	2 6	2
69	Tm	2	2 6	2 6 10	2 6 10 13	2 6	2
70	Yb	2	2 6	2 6 10	2 6 10 14	2 6	2

5. Uses and Industrial Exposure

The largest uses for lanthanides require compounds rather than metals. Most of these applications are for the mixture of lanthanides as they occur in their ores and for cerium compounds. World-wide production of rare-earth oxides (1981) is estimated to be more than 2.5×10^7 kg in total for the rare earths and the U.S. uses more than 1.5×10^7 kg annually. (For comparison, EDS will use less than 1×10^2 kg annually.)

About 25% of the lanthanide chemicals produced are used in carbon-arc lighting applications. Lanthanide-cored carbons are indispensable to the motion picture and printing industries and are used in lithography studios, theatrical lighting, and theater projection. U.S. Army, Navy, and Coast Guard searchlights also use these lanthanide-cored carbons.

Another 25% of the production of lanthanides is used in the form of mixed lanthanide metal (misch metal) and cerium metal. These metals are used in cigarette lighter flints, magnesium alloys, and some of the ferrous alloys. In lanthanide alloy production some applications use lanthanide salts instead of metals.

The third 25% of lanthanide production is used in the glass industry. Didymium (a mixture of neodymium and praseodymium), cerium salts, and some separated lanthanides have important uses in both the coloring and the decoloring of glass. Cerium oxide and some forms of specially prepared lanthanide oxides are widely used in the polishing of spectacle and optical instrument lenses (replacing rouge) and in the surface preparation of mirror glass and other glass specialties.

The remaining 25% of the lanthanide usage is divided among many miscellaneous applications, including phosphors for x-ray screens and television tubes, catalysts, lasers (Stokinger, 1981), and high-temperature superconductors.

The rare earths have been the subject of much research and new uses continue to be found. Much of the information on the toxicology of the rare-earth metals has been gained from evaluation of these materials for medical purposes. For example, cerium oxalate has been found useful for relieving vomiting during pregnancy (Browning 1969) and gadolinium is used as a contrast agent in magnetic resonance imaging.

6. Nonrespiratory Studies

Most of the information on rare earths from animal studies has been obtained from studies of oral, subcutaneous, intraperitoneal, or intravenous administration. For occupational and environmental exposures the applicable studies are those using inhalation and dermal exposures. Information on the toxicity of these materials when they are introduced through nonrespiratory pathways in animals is included here as background information. Information on inhalation is summarized later.

6.1 Animal Studies

The signs and symptoms of high-dose (nonrespiratory) acute toxicity by all the rare earths include ataxia, writhing, slightly labored and depressed respiration, walking on the toes with arched back, and sedation. Death in cats and dogs was due to cardiovascular collapse and respiratory paralysis. Survivors developed generalized peritonitis, adhesions, hemorrhagic ascetic fluid, true granulomatous peritonitis, and focal hepatic necrosis (Bruce, 1963; Haley, 1965, 1966; Arvela, 1977; Venugopal and Luckey, 1978). Table 4 summarizes much of the information from large-dose acute toxicity animal studies and shows the scaled LD_{50} value for a 70-kg human. Table 5 gives animal toxicity information for individual rare-earth elements.

Table 4. Summary of information in the literature regarding acute response of animals for short-term exposure to rare-earth material.

Materials	Ingestion pathway	LD_{50}[a] (mg/kg) (animals)	Scaled LD_{50} mass (mg) for a 70-kg human
Rare-earth nitrates (except Pm)	Intraperitoneal	210 to 480	14,700 to 33,600
Nitrates of Ce, Pr, Nd, Sm, and Er	Intravenous	50 to 70 (male rats)	3,500 to 5,390
		4 to 36 (female rats)	280 to 2,500
Yttrium oxides	Intraperitoneal	500	35,000
Rare-earth nitrates	Oral	3,000 to 5,000	210,000 to 350,000
Rare-earth chlorides	Oral	2,000 to 7,650	140,000 to 530,000
Rare-earth oxides[b] (except Y)	Oral	1,000 to >10,000	70,000 to >700,000

[a]The LD_{50} is the statistically derived single dose of a substance that can be expected to cause death in 50% of the animals (Trevan, 1927).

[b]While rare-earth metals will be used in EDS tests, metal oxides could be formed as a result of off-normal events.

Table 5. Summary of oral animal toxicity measurements for compounds of the individual rare-earth elements (adapted from Rhone-Poulenc, 1986–87).

	Soluble form (LD_{50}) (mg/kg)		Insoluble form (LD_{50}) (mg/kg)
	Nitrate	Chloride	Oxide
Y	Not available	Not available	Not available
La	(Rat) 4,500	(Rat) 4,200	(Rat) >10,000
Ce	(Rat) 4,200 (Rat) 3,600	(Rat) 2,111 (Mouse) 5,277	(Rat) >5,000
Nd	(Rat) 2,750	(Mouse) 5,250 (Mouse) 3,692	(Rat) >1,000[a]
Eu	(Rat) 5,000 (Rat) 5,000	(Mouse) 5,000	(Rat) >1,000[a]
Gd	(Rat) 5,000 (Rat) 3,805	(Mouse) >2,000	(Rat) >1,000[a]
Tb	(Rat) 5,000	(Mouse) 5,100 (Mouse) 3,631	(Rat) >1,000[a]
Dy	(Rat) 3,100	(Mouse) 7,650 (Mouse) 5,443	(Rat) >1,000[a]
Ho	(Rat) 3,000	(Mouse) 7,200 (Mouse) 5,165	(Rat) >1,000[a]
Er	(Rat) >5,000	(Mouse) 6,200 (Mouse) 4,417	(Rat) >1,000[a]
Tm	N/A	(Mouse) 6,250 (Mouse) 4,294	(Rat) >1,000[a]
Yb	(Rat) 3,100	(Mouse) 6,700 (Mouse) 4,836	Not available

[a]There is some experimental evidence that doses between 2,000–10,000 mg/kg have no harmful effects in experimental animals (Sax, 1984).

6.2 Human Studies

The low oral toxicity of the rare earths was demonstrated in an evaluation of their use as a marker in human nutritional studies [Hutcheson *et al.* (1975)]. A sense of the relatively low oral toxicity of the rare-earth metals and their compounds can be gained by a comparison to oral toxicity information on a number of other compounds of which the public is generally aware (Table 6).

Sodium cyanide	(Rat)	6.44
Arsenic trioxide	(Rat)	20
	(Mouse)	45
	(Man)	1.43
Nicotine	(Rat)	50
	(Mouse)	24
Aspirin	(Rat)	1,000
(salicylic acid acetate)	(Mouse)	815
Table salt (sodium chloride)	(Rat)	3,000
	(Mouse)	4,000
Rare-earth oxide	(Rat)	1,000 to >10,000

Table 6. Oral toxicity (LD_{50}) (mg/kg) information for a number of other materials (DHHS–NIOSH, 1986).

For a slightly toxic substance such as a rare-earth oxide ($LD_{50} \geq$ 1000 mg/kg), it is essentially impossible to construct a scenario by which a worker or the public could accidentally ingest or have injected 70,000 mg of rare-earth oxide without their knowledge and ability to obtain medical care. This amount of material (approximately 2.4 ounces of solid material) would be equivalent to a solid lump of material 1 in. square and more than 1/2-in. high (0.6 $in.^3$).

6.3 Conclusions from Nonrespiratory Studies

Because of the very high levels of oral ingestion that can be safely tolerated and the low likelihood of deliberate ingestion or chronic ingestion, incidental oral ingestion is considered to be harmless. It is concluded that the use of rare earths in the EDS test does not represent a health risk due to accidental nonrespiratory uptake.

7. Inhalation Studies

Because of the very high levels of oral ingestion that can be safely tolerated, worker and environmental safety are primarily concerned with accidental and chronic inhalation.

7.1 Animal Inhalation Studies

Guinea pigs daily inhaling mixtures of lanthanides high in fluorides (65% fluorides, 10% oxides, 31% carbon) at 200 to 300 million particles/ft^3 (~31 to 47 mg/m^3) (1- to 2-μm particles) for 3 years showed focal hypertrophic emphysema, regional bronchiolar stricturing, and subacute chemical bronchitis, but no fibrosis or granulomatosis (Schepers, 1955a). A similar experiment with a mixture higher in oxides (39.6% fluorides, 26.4% oxides, and 17% carbon) revealed a less severe reaction with dust entrapped within focal atelectatic areas, but again no fibrosis or substantial chronic cellular reaction (Schepers 1955b).

An 8-month inhalation study compared intratracheal doses of 50 mg Y_2O_3, Ce_2O_3, and Nd_2O_3 in rats (Mogilevskaya, 1963). Ce_2O_3 did not produce serious changes in lung tissue. Nd_2O_3 produced weak to moderate granulomatous and sclerotic granulomatous changes, but at 8 months Y_2O_3 had produced pronounced granulomatous nodules and emphysematous changes. This study subsequently lead to the lowering of the TLV for yttrium from 5 mg/m^3 to 1 mg/m^3 (Stokinger 1981). This study would also indicate that cerium and neodymium oxides are no more injurious than yttrium and may be significantly less toxic. Granuloma formation with inhalation has been confirmed by other relatively high dose studies with rare-earth oxides (Haley, 1979).

Ball (1966) exposed white CFW mice to 30 mg/m^3 of gadolinium oxide for 6 h/day for 20–120 days. This exposure resulted in an increase in pneumonia cases and some microscopic calcification of pleural tissue was noted. No fibrosis or granulomas occurred from this exposure.

Inhaled cerium citrate, chloride, and cerium entrapped in fused-clay particles cleared the body rapidly, with 10% clay, 20% chloride, and less than 30% of the citrate remaining by the end of the 20 days. At 120 days, 25% citrate, 10% chloride, and 2% clay still were present. Ninety percent of the cerium clay that remained was in the lungs. The more soluble cerium citrate and chloride appear more readily in the liver and bones where they apparently are not released so easily. All three are excreted primarily by the feces (90% or more) but also by the urine (10%) (Morgan, 1970).

Palmer (1987) evaluated oxides and chlorides of cadmium, cerium, lanthanum, and neodymium *in vitro* in pulmonary alverlar macrophage culture. Cerium and lanthanum oxides did not produce cytotoxic reactions, but neodymium oxide (LD_{50} = 101 μmoles) did produce cell surface changes. Cadmium oxide (LD_{50} = 15 μmoles) was used for comparison. This study suggests that neodymium oxide may be fibrogenic in inhalation exposures.

7.2 Inhalation Data Gained from Exposure to Humans in an Industrial Environment

There is limited negative human exposure experience in the medical literature and the role of rare earths in the production of pathological lung disease is uncertain. Vague symptoms of nausea and headache have been reported in lithographic workers exposed to cored carbon arc lights (Fairhall, 1957). Heuck (1968) and Cardani (1975) have reported "cerium pneumoconiosis" in lithography workers with similar occupational exposures. Pneumoconiosis has also been reported by Hecht (1980) in dry printing workers. All of these studies are confounded by the complex nature of the exposures and the presence of rare-earth fluoride compounds in the carbon arc. Husain (1980) describes a 34-year-old exposed to a blend of rare earths in a dry concentrate. Profuse nodular shadowing was reported on routine chest x-ray with normal pulmonary function. This case is similar to that reported by Nappee (1972) in which two cerium oxide workers developed a "miliary" pattern on CXR with normal pulmonary function.

Sabbioni (1982), Vocaturo (1983), and Pietra (1985) evaluated the case of a photoengraver exposed to carbon-arcs for 46 years. Chest x-ray showed pulmonary fibrosis and lung and lymph node biopsy showed elevated levels of rare-earth elements compared to autopsy samples from nonexposed controls. Further analysis by neutron activation eliminated fibrosis from radio-thorium as an etiology due to low thorium levels in the tissues. They were unable to establish a causal relationship between rare-earth exposure and pathological pneumoconiosis because of concomitant actions of carbon, other heavy metal dusts, and irritative agents such as oxides of nitrogen or hydrofluoric acid vapors.

The current literature on long-term (20-year) human exposure suggests that rare-earth oxides may cause a benign pneumoconiosis in pure exposure, which is supported by the animal studies of pure rare-earth oxide exposures. (Benign pneumoconiosis is the deposition of material in the lung, visible on x-ray, without any impairment of lung function). Rare-earth halides may be more toxic than the oxides and may require additional care in handling.

7.3 Conclusions from Inhalation Studies

The possible higher toxicity of rare-earth halides, especially fluorides, is not pertinent to EDS because there is no use of any rare-earth halide in the testing.

Animal studies show that two of the rare-earth oxides (cerium and neodymium) are no more toxic than yttrium. The use of the yttrium toxicological standards for safe occupational and public exposure appears properly conservative and appropriate for the evaluation of EDS emissions. (In UCID-21822, the use of this limit is placed in the context of EDS operations.)

The very few human studies that showed any medically significant effects were the results of essentially unmitigated chronic exposures over long periods of time. These studies were further confounded by other factors (e.g., smoking and exposure to other toxic substances).

8. Dermatologic and Ophthalmologic Toxicity

Many rare-earth salts irritate or damage the eyes and abraded skin (Haley, 1961, 1963, 1964, 1965, 1966). Erbium halides irritate intact rabbit skin. Intradermal injections produced foreign body reactions (granulomas) without resorption of the crystalline deposit within a 45-day observation period. The rare-earth halides are highly irritating to the conjunctiva but cause opacification of the cornea only many hours or days after application onto denuded corneas in rabbits (Haley, 1965). Tebrock (1968), in the only human data available, studied a group of workers exposed to yttrium europium vanadate at an average yttrium concentration of 1.4 mg/m^3. The only effects were irritation of the eyes, upper respiratory, and skin, which the authors attributed to vanadium. Thermal injuries to the cornea and skin could occur because of careless handling of mixtures of rare-earth metals that results in a fire caused by their pyrophoric nature.

8.1 Conclusions from Dermatologic and Ophthalmologic Studies

Because rare-earth halides are not used in EDS tests, there is no dermatological and ophthalmological health risk. There is no evidence in the literature that the metals or their oxides have dermatological or ophthalmological health risk.

9. Occupational Exposure Guidance and Worker Protection

The Threshold Limit Value–Time Weighted Average (TLV–TWA) is defined as the time-weighted average concentration for a normal 8-h workday and a 40-h work week to which nearly all workers may be repeatedly exposed, day after day, without adverse effect (ACGIH, 1988). ACGIH (1987, 88) recommends a TLV/TWA of 1 mg/m^3 for yttrium in workplace air.

The Occupational Safety and Health Administration (OSHA) uses the terminology of permissible exposure limit (PEL). The PEL for yttrium is 1 mg/m^3 as an 8-h time-weighted average. The rare earths have such a low level of toxicity that the PEL for yttrium is more than adequate for the other rare earths (Venogopal and Luckey, 1978; Knight, 1988). Table 7 gives information on exposure guidance for a number of commonly used metals and their compounds.

Table 7. TLV/TWAs for representative compounds (AGGIH, 1988).

	mg/m^3
Beryllium	0.002
Cadmium	0.05
Chromium VI	0.05
Cobalt	0.05
Mercury (vapor)	0.05
Quartz (respirable)	0.1
Silver (metal)	0.1
Thallium	0.1
Lead	0.15
Cotton dust	0.2
Chromium III	0.5
Copper (dust)	1.0
Iron salts	1.0
Nickel	1.0
Yttrium	1.0
Tin (metal)	2.0
Grain dust	4.0
Zinc oxide fume	5.0
Nuisance dusts	10.0

Rare-earth elements are used at LLNL with proper industrial engineering controls to keep personnel exposure below the OSHA PEL and ACGIH TLV/TWA of 1 mg/m^3. Industrial hygiene staff ensure that engineering controls operate properly. Personnel protective equipment, protective clothing, and handling tools are used according to NIOSH/ OSHA Guidelines (DHHS-NIOSH 1981). Medical surveillance may be indicated if employees are exposed to potentially hazardous levels.

Worker training programs that instruct workers to refrain from eating or smoking at the work site and to use simple hygiene while working with these materials provides additional mitigation to accidental oral uptake. Respirators are not required during normal operations, but may be required during equipment maintenance operations.

The rare earths will be handled as though they were plutonium while in the EDS equipment to provide the maximum training and engineering evaluation for later plutonium operations. This mitigates against direct exposure to the workers or visitors. When handled outside of EDS or when in support facilities such as Building 161, exposure to the rare-earth metals or compounds will be limited by administrative and engineering controls. There is essentially no scenario for accidental long-term exposure of the public or workers to these materials as part of EDS testing.

Pyrophoric powders are not expected in EDS tests, but established handling procedures that use inert atmosphere mitigate against a spontaneous combustion of pyrophoric powders. On-site medical services, hazards control staff, and in-place safety equipment mitigates against even an extremely unlikely accidental worker or visitor exposure.

9.1 Conclusions from Occupational Exposure Guidance

Equipment and procedures have been designed to ensure that TLV and PEL limits are not exceeded.

Exposures that are maintained at a level below the TLV/PEL value of 1 mg/m^3 should result in no health impact to workers.

Bibliography

1. American Conference of Governmental Industrial Hygienisis (ACGIH), *Documentation of Threshold Limit Values and Biological Exposure Indices* (Cincinnati, OH, 1986), 5th Ed.

2. ACGIH, *Threshold Limit Values and Biological Exposure Indices for 1988–89* (Cincinnati, OH, 1988).

3. Arvela, P., "Toxicity of Rare-Earths," *Prog. in Pharmacology* **2** (3) 73 (1977).

4. Ball, R. A. and Van Gelder, G., "Chronic Toxicity of Gadolinium Oxide for Mice Following Exposure by Inhalation," *Archives of Environmental Health* **13** 601 (1966).

5. Browning, E., *Toxicity of Industrial Metals* (Butterworths, London, 1969).

6. Bruce, D. W. *et al.*, "The Acute Mammalian Toxicity of Rare-Earth Nitrates and Oxides," *Toxicology and Applied Pharmacology* **5** 750 (1963).

7. Cardani, A. *et al.*, "La Pneumoconiosi da Cerio," *Verona Proc. Congr. Naz. di medicina del Lavoro* (Mattioli, Fidenza, 1975) [as cited in Vocaturo, M.D., *et al.*, "Human Exposure to Heavy Metals: Rare-Earth Pneumoconiosis in Occupation Workers," *Chest* **83** (5) 780 (1983)].

8. Chemical Rubber Company (CRC), *Handbook of Chemistry and Physics* (Cleveland, OH, 1988), 59th Ed.

9. Considine, D.M. (Ed.), *Encyclopedia of Chemistry* (Van Nostrand Reinhold, NY, 1984), 4th Ed.

10. DHHS-NIOSH, *Occupational Health Guidelines for Chemical Hazards*, DHHS-NIOSH Publ. No. 81-123 (1981).

11. DHHS-NIOSH, *Registry of Toxic Effects of Chemical Substances*, DHHS-NIOSH Publ. No. 86-103 (1986).

12. Fairhall, L.T., *Industrial Toxicology* (Williams and Wilkins, Baltimore, MD, 1957), 2nd Ed., pp. 67–68.

13. Haley, T.J. *et al.*, "Toxicology and Pharmacological Effects of Gadolinium and Samarium Chlorides," *British Journal of Pharmacology* **17** 526 (1961).

14. Haley, T.J. *et al.*, "Pharmacology and Toxicology of Terbium, Thulium, and Ytterbium Chlorides, *Toxicology and Applied Pharmacology* **5** 427 (1963).

15. Haley, T.J. *et al.*, "Pharmacology and Toxicology of Praseodymium and Neodymium Chlorides, *Toxicology and Applied Pharmacology* **6** 614 (1964).

16. Haley, T.J., "Pharmacology and Toxicology of Rare-Earth Elements," *Journal of Pharmaceutical Sciences* **54** (5) 663 (1965).

17. Haley, T.J. *et al.*, "Pharmacology and Toxicology of Dysprosium, Holmium, and Erbium Chlorides, *Toxicology and Applied Pharmacology* **8** 37 (1966).

18. Haley, T.J., "Toxicology," in *Handbook on the Physics and Chemistry of Rare Earths* (North-Holland, NY, 1977), K.A. Gschneider and L. Eyring, Eds., Vol. 4.

19. Hecht, F.M. and Wesch, H., "Pneumokoniose Prat Pneumol.," *Beitrag zum rontgenologischen Bild der cer* **34** 169 (1980).

20. Heuck, F. and Hoschek, R., "Cer-Pneumoconiosis," *American Journal of Radiology* **104** 777 (1968).

21. Husain, M.H. *et al.*, "Rare-Earth Pneumoconiosis," *Journal of Society of Occupational Medicine* **30** 15 (1980).

22. Hutcheson, D.P. *et al.*, "Studies of Nutritional Safety of Some Heavy Metals in Mice," *Journal of Nutrition* **105** 670 (1975).

23. Knight, A.L., "The Rare Earths" in *Occupational Medicine* (Yearbook Medical, Chicago, 1988), C. Zenz, Ed., pp. 609–613.

24. Mogilevskaya, O.Y. and Raikhlin, N.T., "Rare-Earth Metals" in *Toxicology of Rare Metals* (Gsudarstyennoe Izdatelstvo Meditsinskoi Literatury, Moscow, 1963), Z.I. Izraelson, Ed., pp. 195–208.

25. Morgan, B.N. *et al.*, "Influence of Chemical State of Cerium 144 on its Metabolism Following Inhalation by Mice," *American Industrial Hygiene Association Journal* **31** 479 (1970).

26. Nappee, J. *et al.*, "Pneumoconiose au Cerium." *Archives of Mal Prof.* **33** 13 (1972).

27. Palmer, R.J. *et al.*, "Cytotoxicity of the Rare-Earth Metals Cerium, Lanthanum, and Neodymium *in Vitro*," *Environmental Research* **43** 142 (1987).

28. Pietra, R. *et al.*, "Trace Elements in Tissues of a Worker Affected by Rare-Earths Pneumoconiosis," *Journal of Radiology and Nuclear Chemistry* **92**(2) 247 (1985).

29. Rhone-Poulenc Mineral Fine, *Rare-Earth Reminder* (Paris, 1986–87).

30. Sabbioni, R. *et al.*, "Long Term Occupational Risk of Rare-Earth Pneumoconiosis," *Science for the Total Environment* **26** 19 (1982).

31. Sax, N.I., *Dangerous Properties of Industrial Materials* (Van Nostrand Reinhold Co., NY, 1984), 6th Ed.

32. Schepers, G.W., "The Biological Action of Rare Earths II: The Experimental Histopathology Produced by a Blend Having a Relatively High Fluoride Content," *AMA Archives of Industrial Health* **12** 306 (1955a).

33. Schepers, G.W., "The Biological Action of Rare Earths I: The Experimental Histopathology Produced by a Blend Having a Relatively High Oxide Content," *AMA Archives of Industrial Health* **12** 301 (1955b).

34. Stokinger, H.E., "The Metals" in *Industrial Hygiene and Toxicology* (Interscience Publishers, NY, 1981) F.A. Patty, Ed., 3rd Ed.

35. Tebrock, H.E. and Machle, W., "Exposure to Europium Activated Yttrium Orthovanadate," *Journal of Occupational Medicine* **10** 692 (1968).

36. Trevan, J.W., "The Error of Determination of Toxicity" in *Proceedings of the Royal Society of London*, Biology **101** 483 (1927).

37. Venugopal, B. and Luckey, T.D., *Metal Toxicity in Mammals* (Plenum Press, NY, 1978),Vol. 2, pp. 131–157.

38. Vocaturo, M.D., *et al.*, "Human Exposure to Heavy Metals: Rare-Earth Pneumoconiosis in Occupation Workers," *Chest* **83** (5) 780 (1983).