



ADDENDUM TO THE TOXICOLOGICAL PROFILE FOR THORIUM

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ADDENDUM FOR THORIUM

Supplement to the 1990 Toxicological Profile for Thorium

Background Statement

This addendum to the [Toxicological Profile for Thorium](#) supplements the profile that was released in 1990.

Toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). CERCLA mandates that the Administrator of ATSDR prepare toxicological profiles on substances on the CERCLA Priority List of Hazardous Substances and that the profiles be revised “no less often than once every three years.” CERCLA further states that the Administrator will “establish and maintain inventory of literature, research, and studies on the health effects of toxic substances” [Title 42, Chapter 103, Subchapter I, § 9604 (i)(1)(B)].

The purpose of this addendum is to provide to the public and other federal, state, and local agencies a non-peer reviewed supplement of the scientific data that were published in the open peer-reviewed literature since the release of the profile in 1990.

Chapter numbers in this addendum coincide with the [Toxicological Profile for Thorium](#) (1990). This document should be used in conjunction with the profile. It does not replace it.

2. HEALTH EFFECTS

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

Many of the studies evaluating the health effects of thorium (Th) involved the intravascular injection of a colloidal suspension form of $^{232}\text{ThO}_2$ termed Thorotrast. Thorotrast was specifically prepared as an injectable contrast agent for medical x-ray imaging of the body during the period 1928-1954. Although the colloid contained different size particles, some manufacturers filtered out the large particles leaving an average size of 10 nm (Dalheimer et al. 1988), i.e., Thorotrast was a nanomaterial. Its manufacture and use ended when delayed adverse health effects were recognized and attributed to its use. These effects included bone marrow insufficiency and hemangioendothelioma (sometimes termed thorotrastosis) and cancer. Thorotrast has unique physico-chemical characteristics which enable it to distribute to bone marrow and have essentially complete retention. This, along with the use of an intravenous or intravascular route of exposure make Thorotrast dissimilar to non-colloidal thorium, and therefore make Thorotrast-related data of limited use for assessing thorium exposure from environmental and occupational sources. As such, Thorotrast studies are of limited usefulness in understanding the potential health effects from public and occupational exposure to thorium. They are included in this addendum to add follow-up to information presented in the Toxicological Profile for Thorium (ATSDR 1990).

2.2.1 Inhalation Exposure

2.2.1.1 Death

Liu et al. (1992) published follow-up results from assessment of mortality among former workers in a thorium-processing and gas mantle production plant in the United States; earlier reports (Polednak et al. 1983; Stehney et al. 1980) were summarized in the Toxicological Profile for Thorium (ATSDR 1990). Among 3,119 male workers, a significantly elevated standardized mortality ratio (SMR) was reported for all causes of death (SMR = 1.12; 95% confidence interval [CI] 1.05–1.21), including an elevated rate of motor vehicle accidents. However, among 677 female workers there was an apparent positive health impact with a significantly reduced SMR for all causes of death of 0.74 (95% CI 0.63–0.86) (Liu et al. 1992). It is unclear how prior exposure to thorium might impact driving skills, other than perhaps effects on neuromuscular coordination or some other physiological process that has an effect on response times to external stimuli.

2.2.1.7 Genotoxic Effects

Thorium has been reported as genotoxic to lymphocytes in occupational workers. The potential for this to be due to chemical interaction among thorium, cerium, and lanthanum, which are present in monazite sand, was evaluated *in vitro* (see Section 2.6 below).

2.2.1.8 Cancer

For 20 years, Stehney and co-workers studied the health effects and toxicokinetics of occupational exposure in former thorium workers at the Lindsay operational facility of the Kerr-McGee Chemical Company. The study population included 3200 men (who extracted and purified thorium and rare earth metals from monazite ores at the facility's thorium mill in Chicago and West Chicago, IL from 1932-1973) and 700 women (who prepared thorium lantern mantles in the Morris, IL factory from 1936-1947). Stehney et al. (1980) reported excess deaths from respiratory disease (33 vs. 25.2), lung cancers (31 vs. 21.6), pancreatic cancer (9 vs. 4.5), and rectal cancer (6 vs. 3.2), with the only cancer association between job type and length being pancreatic cancer in males who had worked >1 year. Those results may have been affected by co-exposure to other substances in the process streams (e.g., silica dust, which is now recognized by the International Agency for Research on Cancer as a human carcinogen (IARC 1997)) and a high rate of cigarette smoking (Stehney et al. 1980). The 1990 Toxicological Profile for Thorium (ATSDR 1990) addressed only pancreatic cancer (but not the other cancers). Also, it correctly questioned, but for the wrong confounding substance, the causal relationship between cancer and worker exposures. The profile considered that radon-222 (^{222}Rn) was a confounder and that exposure was unrelated to thorium; this isotope is a decay product of ^{232}Th (ATSDR 1990) and is an anticipated thorium-related analyte in breath samples. Stehney (1999) assessed the thorium distribution in autopsy samples from 4 of the mill workers, estimated that committed doses from thorium exposure to the workforce would not have exceeded an average 0.005 Sv, and concluded that occupational exposures to workers at the refinery likely had no significant impact on their cancer risk.

Liu et al. (1992) published follow up results from assessment of mortality among former workers in a thorium-processing and gas mantle production plant in the United States; earlier reports (Polednak et al. 1983; Stehney et al. 1980) were summarized in the Toxicological Profile for Thorium (ATSDR 1990). For 3,119 male workers, significantly elevated SMRs were noted for all cancers (SMR = 1.23; 95% CI 1.04–1.43) and lung cancer (SMR = 1.36; 95% CI 1.02–1.78). However, for 677 female workers, there was significantly reduced SMRs for all malignant neoplasms (SMR 0.53, 95% CI 0.35-0.78) and circulatory diseases (SMR 0.66, 95% CI 0.53-0.82). Explanations offered regarding the better results for

women included possible non-detrimental effects from radiation exposure, a healthy worker effect, and different jobs (with men engaged with thorium extraction and women making incandescent gas mantles).

Chen et al. (2003) and Chen et al. (2004) reported results of a 20-year follow up study on health effects in workers with potential for long-term exposure to thorium and silica dusts in ore (0.04% ThO₂, 10% SiO₂) plus the progeny of thoron (²²⁰Rn) at a rare-earth iron mine in China. As of 2001, a total of 6,983 miners and staff members had been identified, 3,016 of whom were considered to have been exposed to thorium dust. Dust-exposed miners were estimated to have a Th lung burden of 1.6 Bq versus 0.3 Bq for those not exposed to dust. The 27 lung cancer deaths among dust-exposed workers were associated with an SMR of 6.13 (95% CI 4.41-8.52) while the 8 deaths from workers not exposed to dust had an SMR of 1.90 (95% CI 0.94-3.84). Considering the ore dust content and cigarette smoking history, the estimated breakdown of the 27 deaths was 1 from Th, 2 from thoron progeny, 12 from cigarette smoke, and 12 from silica.

2.2.4 Other Routes of Exposure

Most epidemiological data for thorium deal with health effects following intravenous or intravascular injection of Thorotrast, a colloid containing ²³²ThO₂, which was used as a radiographic contrast medium between 1928 and 1955 (ATSDR 1990). Results of most recent follow up of Thorotrast patients provide support to the earlier findings and are briefly summarized below. Studies using Thorotrast have limited relevance to potential health effects from environmental and occupational exposures to thorium.

Results from animal studies that employed the intravenous injection route of exposure to thorium are summarized in this section as well.

2.2.4.1 Death

No information regarding death in humans from exposure to thorium and its typical compounds was found. Follow up reports of patients who had been administered Thorotrast intravascularly found significant associations between Thorotrast exposure and mortality from all causes combined, as well as specific site cancers (particularly liver, gall bladder, and leukemia) and non-neoplastic diseases (most commonly liver cirrhosis) (Andersson et al. 1995a; Andersson et al. 1993a; Andersson et al. 1993b; Andersson and Storm 1992; Andersson et al. 1994b; Andersson et al. 1995c; ATSDR 1990; Becker et al. 2008; Kido et al. 1999; Martling et al. 1999; Mori et al. 1999a; Mori and Kato 1991; Mori et al. 1999b; Travis et al. 2003; Travis et al. 2001). Studies on cancer are addressed in Section 2.2.4.8.

Bruenger et al. (1991) reported average survival of 4,091 days (standard error [SE]±319 days) among a group of 11 beagle dogs following intravenous injection of 0.56 ± 0.03 kBq (18 ± 1 pg) $^{228}\text{Th}/\text{kg}$ (form not reported); average survival of a group of 11 control dogs was $4,824\pm 355$ days. Lloyd et al. (1995) reported significantly ($p<0.001$) reduced survival in a group of 81 male and female beagles following intravenous injection of ^{228}Th (form not reported) at $0.06\text{--}102$ kBq/kg. Mean survival among the ^{228}Th -treated dogs was 9.2 ± 4.15 years compared to mean survival of 13.17 ± 2.64 years for a group of 133 control dogs. Survival of both groups greatly exceeded the typical 5.5 years for privately owned dogs and was attributed to professional animal management.

2.2.4.2 Systemic Effects.

Cardiovascular Effects. No updated information was found on cardiovascular effects from exposure to thorium, other than for Thorotrast. Schlemmer et al. (2000) assessed the development of paravascular Thorotrast deposits (granulomas) and associated clinical symptoms in a subgroup of 899 patients from the German Thorotrast study who had been injected with Thorotrast in the 1930s and 1940s with a greater than 50-year follow-up period after Thorotrast administration. The granulomas were considered to have been the result of accidental extravascular deposition of Thorotrast during the intravascular injection procedure. A total of 245 out of the 899 patients exhibited granulomas, which caused increased frequency of a variety of symptoms caused by fibrosis, nerve paralysis, and vascular changes (compared to those reported for a group of 662 control subjects). Clinical symptoms were dependent on the location and extension of granulomas and appeared from 10 to 30 years following Thorotrast treatment. Symptoms that included arterial compression, occlusion, and rupture were associated with granulomas in close proximity to vascular tissue.

Hepatic Effects.

Ali et al. (2014) evaluated the cellular effects of thorium nitrate on human-derived liver cells (HepG2). Exposure for 72-h to $0.1\text{--}10$ μM concentrations of thorium increased proliferation by 40-60%, while exposure to ≥ 50 μM solution was ineffective. Effects of the lower doses were then evaluated. To understand the pathways involved, cells pretreated with pathway-specific inhibitors (PI3K or JNK-MAPK) showed reduced thorium-related proliferation, while thorium increased the cellular levels of phospho-Akt (by 35%) and phospho-JNK (by 100%). Thus, PI3K mediated the activation of phospho-Akt and phospho-JNK. Thorium also affected the cell cycle. When thorium-treated cells were exposed to tritium-labeled thymidine, an increased fraction underwent DNA replication, the fraction of cells at G1 was reduced, and the fractions at S-phase and G2-M phase were increased. There was an

associated 45% increase in cyclin-E levels. Exposure of the cells to a neutralizing antibody to insulin-like growth factor 1 receptor (IGF-1R) reduced proliferation, indicating that thorium-related proliferation involved an IGF-1R-mediated signaling mechanism.

Follow up reports (van Kaick et al. 1999; van Kaick et al. 1991) of the German Thorotrast study (van Kaick et al. 1983) summarized in the Toxicological Profile for Thorium (ATSDR 1990) provide more recent data on liver cirrhosis in patients who had received intravascular injection of Thorotrast. In the most recent report (van Kaick et al. 1999), liver cirrhosis had been diagnosed in 372 of 2,326 Thorotrast patients (16%) and 50 of 1,890 control subjects (2.6%). Liver cancer in combination with liver cirrhosis was noted in about 30% of the Thorotrast patients with liver tumors. Liver cirrhosis was noted in 13% of those Thorotrast patients who had not developed liver cancer.

2.2.4.3 Immunological Effects

No updated information was found on immunological effects from exposure to thorium, other than for Thorotrast. Abe et al. (1999) observed significantly elevated plasma IgM class anti-lipid A antibody activity in Thorotrast patients compared to controls. In addition, counts of CD 11+ and CD 57+ lymphocytes, which correspond to monocytes and natural killer cells, respectively, were significantly increased in the Thorotrast patients.

2.2.4.4 Neurological Effects

Kumar et al. (2009) exposed female Swiss albino mice *i.p.* to 5 mg thorium/kg/day as thorium nitrate and evaluated its neurochemical and neurobehavioral effects. A significant linear correlation was found between thorium concentration and an increase in acetylcholinesterase (AChE) specific activity for those portions of the brain that were studied. Increases in concentration and AChE activity were accompanied by increases in lipid peroxidation, suggesting a role for thorium in inducing oxidative stress. The same dose also resulted in a 1-day delay in learning a conditioned avoidance response to electrical shock inside a shuttle box apparatus. Control and exposed animals began exhibiting the anticipated response on day 4 and 5, respectively, and learning improved linearly at the same rate in both groups for the next 2-3 days.

Schlemmer et al. (2000) provided an update on the neurological effects from exposure to Thorotrast. Symptoms that included pain, restriction of movement, and paresis or paralysis of cervical sympathetic or caudal cranial nerves associated with granulomas in close proximity to nerves were reported in a group of 899 angiography patients who had been injected with Thorotrast in the 1930s and 1940s. These effects

generally occurred in the neck, shoulder-arm, or pelvis-limb region in the immediate vicinity of injection sites where needle head slip during injection deposited Thorotrast outside the blood vessel. This occurred in 27% of patients studied. Thorium deposits were coarsely located using screen-film radiography taken in orthogonal planes and recognized as inhomogeneous opacifications in soft tissue along with calcification. Attempts to resect Thorotrast deposits were largely unsuccessful due to poor post-surgical outcomes and related deaths. By 10-25 years post-exposure (average 19 years), 50% of those patients were symptomatic and the extent of deposits exceeded 10 cm². Refer to Cardiovascular Effects in Section 2.2.4.2 for a more detailed study description.

2.2.4.7 Genotoxic Effects

No updated information was found on genotoxic effects from exposure to thorium, other than for Thorotrast.

Kyoizumi et al. (1992) and Umeki et al. (1991) reported significantly increased frequencies of mutant T lymphocytes defective in T-cell receptor gene expression in the peripheral blood of Thorotrast and ¹³¹I patients, but not in atomic bomb survivors in Japan. The authors suggested that mutation frequency might be used as a radiation dosimeter to identify individuals who recently had been exposed to high doses of radiation, and noted that the analysis required only 1 mL of blood, commercially-available antibodies, and equipment available in many laboratories.

Radiation-induced increased frequencies of chromosomal aberrations (multicentrics and centric and acentric rings) but not mutations have been reported in peripheral blood lymphocytes at the hypoxanthine phosphoribosyltransferase locus (Littlefield et al. 1997; Platz et al. 2000) or in bone marrow hemopoietic stem cells (Tanosaki et al. 1999) of Thorotrast patients.

Andersson et al. (1995b) evaluated the potential for alpha radiation to increase the rate of p53 point mutations in Thorotrast patients. Tissues containing 18 hepatocellular carcinomas, 9 cholangiocarcinomas, and 9 hepatic angiosarcomas were evaluated, with attention being paid to codon 249 of the p53 gene. No high scores were observed for p53 protein expression, and the scores appeared to be lower than those reported for European hepatocellular carcinomas.

Gonzalez-Vasconcellos et al. (2011) evaluated mice with Rb1 tumor suppressor gene and p16 germline defects to identify their impact on osteosarcomagenesis induced by thorium. Female mice (n=42-80) in

each of three strains were injected with 185 Bq/g of ^{227}Th , tumors were assessed over more than 400 days, and DNA of healthy and tumor tissues were assessed for the allelic ratio of Rb1 to p16 loci. Rb1 germline defects resulted in an increased predisposition for thorium-induced osteosarcoma. However, a p16 defect tends to shorten tumor latency, in the later stages of tumor promotion, rather than affecting susceptibility.

2.2.4.8 Cancer

Numerous reports of cancer in patients who had been administered Thorotrast intravascularly, some with paravascular deposits due to needle penetration of the vein, have been published subsequent to those available for the Toxicological Profile for Thorium (ATSDR 1990). The more recent reports include follow up of patients from Japan (Ishikawa et al. 1992; Ishikawa et al. 1995; Kido et al. 1999; Mori et al. 1999a; Mori and Kato 1991; Mori et al. 1999b; Sasaki et al. 1999), Denmark (Andersson et al. 1995a; Andersson et al. 1993a; Andersson et al. 1994a; Andersson et al. 1993b; Andersson and Storm 1992; Andersson et al. 1994b; Andersson et al. 1995c; Visfeldt and Andersson 1995), Portugal (dos Santos Silva et al. 1999; 2003), Sweden (Martling et al. 1999; Nyberg et al. 2002), Germany (Schlemmer et al. 2000), and an international cohort of patients from Denmark, Sweden, and the United States (Travis et al. 2003; 2001). These studies confirm significant associations between Thorotrast treatment and risk of developing cancer, particularly liver cancer, leukemia, and cancer of the gall bladder; in the case of paravascular puncture deposition, the primary association was with malignant tumors at edges of granulomas in the deposition field. Risks increased significantly with time since first administration of Thorotrast and with cumulative α -particle dose.

Schlemmer et al. (2000) conducted a large German follow-up study of Thorotrast patients for which needle slip during injection resulted in paravascular deposits of Thorotrast in 245 of 899 patients studied. During the follow-up period, deaths had been attributed to radiation fibrosis (6), malignant tumors at edges of granulomas (4), squamous cell carcinoma of the parotid gland (2), lymphoepithelial carcinoma of the nasopharynx (1), and soft tissue sarcoma of the groin (1). The authors considered the low rate of Thorotrast-related soft tissue sarcomas in humans to be unexpected, since a study on dogs by Lloyd et al. (1995) had reported that such effects occurred frequently in Thorotrast-treated animals but not in those exposed only to ^{228}Th . The nasopharyngeal cancer could have been associated with exhaled ^{220}Rn , a decay progeny of ^{232}Th , comparable to cancers of the paranasal sinus cavities of radium dial painters that were attributed to ^{222}Rn progeny of ^{226}Ra that they ingested. Among 851 Thorotrast patients examined at death, no statistically significant difference in age at death was found between those with (n=228) or

without (n=623) observable paravascular deposits. Becker et al. (2008) provided an update of the German Thorotrast cohort through 2004, at which time 9 of the 2326 exposed individuals and 151 of the 1890 control subjects were still alive. For this group, Thorotrast exposure increased overall mortality as a function of time since first exposure, and it shortened life an average of 14 years. SMR values were elevated (287 for males and 387 for females versus 153 and 212 for respective controls), primarily due to cancers of the liver and bile ducts (SMR = 16,695 for males and 12,680 for females versus 238 and 439 for respective controls). Relative risks were elevated for other effects as well in males (RR = 10.2 for leukemia, 9.2 for multiple myeloma, and 8.1 for gall bladder cancer) and in females (RR = 17 for brain and nervous system cancers, and 5.3 for malignancies of eye, brain, and nervous system).

Yamamoto et al. (2009) hypothesized a mechanism for Thorotrast-induced carcinogenesis. The evaluation used an autopsy study of 168 histologically confirmed Thorotrast cases in Japan. It focused on cases of intrahepatic cholangiocarcinoma (ICC), since ICC was not associated with hepatic viruses and appeared to come from a single stem cell type from which hepatocytes and bile duct epithelial cells arise. Five Thorotrast-ICC cases were identified through autoradiography of pathology slides as covering low, moderate, and high levels of Thorotrast deposition; these were compared with 5 non-Thorotrast-ICC controls. Thorotrast deposited primarily in the portal area at approximately 50-times the concentration in other areas within the liver. It was hypothesized that each cell which develops into a tumor is first hit by one alpha particle and then must be removed from the sphere of further alpha particle exposure to preclude receiving a lethal radiation dose. Movement could be by slow cell migration or removal of the thorium itself by macrophagic action. The authors considered this to be consistent with a 24-year minimum latency for Thorotrast-related cancer induction. In a subsequent study, Yamamoto et al. (2010) found that the ratio of $^{228}\text{Ra}/^{232}\text{Th}$ was higher in ICCs than in angiosarcomas and concluded that this supported their mobility hypothesis. However, the hypothesis did not consider that ICC rates were not elevated in distal tissues where lower Thorotrast concentrations would have likely resulted in fewer multiple alpha interactions with individual cells.

Bruenger et al. (1991) observed bone tumors in 5 of 11 beagles following a single intravenous injection of $0.56 \pm 0.03 \text{ kBq } ^{228}\text{Th}/\text{kg}$. The study authors stated that bone tumor induction was clearly elevated in the ^{228}Th -treated dogs, but did not report bone tumor incidences in a group of 11 control dogs. Lloyd et al. (1995) observed significantly ($p < 0.0001$) elevated incidences (44 of 76 treated dogs versus 1 of 131 control dogs) of bone tumors in a group of at-risk beagle dogs following intravenous injection of ^{228}Th in the range of 0.06–102 kBq/kg. Comprehensive soft tissue examinations revealed no significantly increased incidences of treatment-related soft tissue tumors.

Gonzalez-Vasconcellos et al. (2011) injected 42-80 female mice of 3 strains with 185 Bq ^{227}Th /g body weight. Osteosarcomas developed in 25 of 80 BCF1 mice with 290-766 day latencies. The tumors were located in extremity bones (32%), ilium and sacrum (28%), vertebrae (28%), and skull (12%).

In a study designed to assess the separate and combined effects of exposure to quartz aerosols and intravenously-injected Thorotrast on tumor induction in rats, Spiethoff et al. (1992) administered enriched Thorotrast (1.8 kBq ^{228}Th) to female Wistar rats, some of which had been exposed to silica dust at 0, 6, and 30 mg/m³ for 29 days. Among the rats administered Thorotrast in the absence of prior exposure to the quartz aerosols, 3 of 87 unexpectedly developed lung tumors (perhaps associated with exposure to the ^{220}Rn progeny); no lung tumors were seen in 85 untreated control rats. Forty-two of the 87 rats receiving Thorotrast treatment only also exhibited liver and spleen tumors compared to 5 of 85 in untreated controls. The study found an association between lung cancer induction and co-exposure to Thorotrast and silica dust, which resulted in increased tumor rate (observed/expected was 1.508 and 1.724 in the respective low and high silica groups) and shortened latency by up to 5 months. The authors reported increased tumor rats due only to silica, and an unexpected rate of lung tumors in the Thorotrast only group. The finding of lung cancers from quartz only exposures presages the conclusion by IARC that silica dust is carcinogenic to humans (ATSDR 2012; 2013; IARC 1997).

2.3 TOXICOKINETICS

2.3.2 Distribution

Glover et al. (2001) reported on the distribution of ^{232}Th activity in the tissues of a whole body donor (with no known occupational exposure to thorium) to the United States Transuranium and Uranium Registries. The whole body activity (310 mBq or 76 μg based on a specific activity of 4080 Bq/g) was distributed among the respiratory system (39.1%), skeleton (34.2%), muscle (16.6%), skin (8.39%), tracheobronchial lymph nodes (4.13%), CNS (0.329%), liver (0.22%), kidneys (0.11%), spleen (0.065%), and other soft tissues combined (1.1%). The percentages total 104%, perhaps indicating that the thorium content of tracheobronchial lymph nodes was included with the respiratory system entry.

Iyengar et al. (2004) estimated contents of several elements, including thorium, in selected organs of the adult Asian population using measured data from road accident victims in China, India, the Philippines, and Republic of Korea who had been healthy prior to accidental death. Reported thorium contents ranged from 3.96 to 22.1 μg (median 14.45 μg) in the skeleton, 0.89 to 7.79 μg (median 3.21 μg) in the lung, and

0.12 to 0.53 μg (median 0.23 μg) in the liver. The thorium content in the skeleton and liver was considered to have resulted from the ingestion of thorium, whereas inhalation of ambient thorium dust was thought to have been the major route of exposure for the thorium content in the lungs.

Harley and Fisenne (1990) assessed the distribution of uranium and thorium in vertebra (highly trabecular bone), rib (a mixture of trabecular and cortical bone), and long bone shafts (highly cortical bone) from skeletal remains of three human donors. Respective mean activity concentrations in vertebra, rib, and long bone shaft were 0.063, 0.083, and 0.044 Bq/kg for ^{230}Th , and 0.048, 0.045, and 0.030 Bq/kg for ^{232}Th .

Kumar et al. (2009) studied the distribution of thorium in the brains of female Swiss albino mice following oral exposure of 8 animals for 30 days to 5 mg thorium/kg/day as thorium nitrate pentahydrate. Thorium distributed nonuniformly within the brain following the order cerebellum (1.2%) > cortex (0.8%) > hippocampus (0.66%) > striatum (0.4%).

2.3.2.1 Inhalation Exposure

Chen et al. (2003) estimated average thorium lung burdens of 1.60 Bq in a group of 638 rare-earth miners in China who were considered to have experienced occupational exposure to thorium dust; an average thorium lung burden of 0.30 Bq was estimated for a group of 143 workers at the same mine who were classified as not exposed to thorium dust. The estimates of lung burdens were based on measurements of exhaled thoron (^{220}Rn) activity.

Jaiswal et al. (2004) assessed thorium lung burden and total body thorium content in 5 workers employed for 10–32 years in a plant that processed thorium concentrate. Average thorium activity measured in various departments of the plant was generally lower than 0.12 Bq/m³ (range 0.03–0.49 Bq/m³). Lung and whole body thorium contents were estimated from results of *in vivo* gamma counting of ^{228}Ac and ^{208}Tl ; limits of detection for thorium in the thoracic area and whole body were 12 and 52 Bq, respectively. Measured thorium lung burden ranged from 15 to 67 Bq; total body thorium content ranged from <52 Bq to 168 Bq.

Hewson and Fardy (1993) reported blood and urine thorium concentrations ranging from 170 to 2,000 ng/L (geometric mean 480 ng/L; geometric standard deviation [gsd] = 1.7, n=25) in the serum and 3-210 ng/L (geometric mean 31 ng/L, n=32) in the urine of mineral sands workers in Western Australia. The

geometric means of unexposed workers were 320 ng/L for serum and 5 ng/L for urine. Based on periodically-recorded data regarding alpha radioactivity in the workplace air and historical worker data, the study authors calculated a geometric mean ^{232}Th intake of 0.4 Bq/day (gsd = 1.7 Bq/day) and geometric mean exposure time period of 1,597 days for the 25 workers. Neither serum nor urine concentrations correlated with cumulative exposures, but serum levels were less variable and considered to be a more reliable indicator of exposure.

Stehney (1999) measured ^{232}Th concentrations in human autopsy tissue samples from 4 thorium mill workers, including a millwright and 3 laborers. Those values were used to compare 2 predictive dosimetry models (one based on ICRP Report No. 30, the other based on ICRP Reports No. 68 and 69), and the latter was found to be more accurate. Stehney and Lucas (2000) later reported additional analytical results for the same 4 workers and an additional laborer. The ^{232}Th concentration (in mBq per gram of wet tissue) ranged from 0.009–0.068 for kidneys, 0.015–0.68 for liver, 0.14–1.19 for bones, 0.97–5.8 for spleen, 0.17–79 for lungs, and 3.9–1210 for pulmonary lymph nodes. Distribution was higher in lower portions of the lung (possibly due to settling) and higher in vertebrae than in other bones. Lung levels remained high for decades after exposure ended, indicating that actinides were retained with a much longer half-time than the 500 days recommended by ICRP Publication No. 30, but results were not sufficient to recommend a new value. After extended periods, the fraction of thorium remaining in bone, liver, and lungs were comparable between workers and the general population.

2.3.2.4 Other Routes of Exposure

Kumar et al. (2012) assessed the distribution of thorium in liver and blood of rats injected i.v. with 0.6 mg thorium/kg as thorium nitrate. After 24 hours, 42% of the thorium was in retained the liver and 12% was in the blood.

The distribution of Thorotrast-derived thorium activity in organs from a female subject who had been injected with Thorotrast 36 years earlier has been evaluated using autopsy tissues from the U.S. Transuranium and Uranium Registry (Kathren and Hill 1992; McInroy et al. 1992; Priest et al. 1992). More than 90% of the thorium was found in the reticuloendothelial system which includes liver (approximately 44–47% of the total), skeleton (32–35%), spleen (11–13%), and lymph nodes (0.28–0.65%). The distribution of Thorotrast is hypothesized to follow the order of cardiac fractional output to the organs (25% for liver, 5% each for bone marrow and spleen, and <1% for lymph nodes); in the current case, it was 44% in liver, 32% in bone, 12% in spleen, 3% paravascularly at the injection site, and 0.4% in

lymph nodes. The resulting tissue concentrations and radiation doses would be proportional to distribution and inversely proportional to tissue mass, such that red bone marrow (primarily in the pelvis) and liver receive the largest mass of Thorotrast, while spleen receives the largest radiation dose. Radiation absorbed doses and equivalent doses to the female subject were estimated for spleen (121 Gy, 2420 Sv, resulting in hyposplenism), liver (15Gy, 300 Sv), skeleton (4 Gy, 80Sv), and the injection site granuloma or Thorotrastoma (16 Gy, 320 Sv) (Kathren and Hill 1992; McInroy et al. 1992). Priest et al. (1992) reported that Thorotrast does not distribute uniformly in liver and bone. Its ^{232}Th radioactivity in bone marrow was largely restricted to areas of cellular bone marrow where it was found throughout the red marrow tissue and concentrated within cells that were commonly aggregated within focalized areas of the marrow. Total bone concentrations of ^{232}Th from highest to lowest were in the pelvis and vertebrae, ribs, upper leg, shoulder and skull, and other extremities. However, disequilibrium in the ^{228}Th : ^{230}Th ratio demonstrates some mobility of the more soluble ^{228}Ra intermediary isotope allowing the ^{228}Th progeny to deposit on distal bone surfaces, such as fibula that has little red marrow. This is consistent with thorium being a bone surface seeker (Lloyd et al. 1984) while colloidal Thorotrast enters the marrow cavities. Concentrations were sufficient for gamma radiation levels to be measured with a portable Geiger-Mueller counter. Significant deposits were not found in fatty yellow marrow (Kathren and Hill 1992).

Humphreys et al. (1998) injected 4 monkeys with Thorotrast to assess any inhomogeneities in bone marrow distribution. Thorotrast was found to evenly distribute in the red marrow at 1 week post-injection. However, Priest et al. (1992) found that after 3–4 years, Thorotrast was deposited as conglomerates within macrophages, similar to the aggregations observed in the red bone marrow of the human autopsy case.

2.3.3 Metabolism

The 1990 Toxicological Profile for Thorium (ATSDR 1990) stated that transferrin has been considered to play a major role in the transport and cellular uptake of thorium, but that thorium can be displaced or its uptake blocked, and the mechanism is unknown. Jeanson et al. (2010) assessed the pH-dependence of thorium binding to transferrin in vitro. They reported that Th(IV) (unlike tetravalent Pu and Np) was never completely complexed to transferrin over the pH range studied, and especially below pH 7. They suggested that a relatively large ionic size, coupled with a relatively weak hydrolysis constant, allows thorium to be easily displaced from transferrin or blocked from interaction. This is consistent with the transferrin pH cycle.

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

Hewson and Fardy (1993) reported thorium concentrations ranging from 3 to 210 ng/L (geometric mean 31 ng/L; geometric standard deviation 2.6) in the urine of 34 mineral sands workers in Western Australia. It was estimated that urinary excretion averaged 2.5% of the thorium body burden. Based on periodically-recorded data regarding alpha radioactivity in the workplace air and historical worker data, the study authors calculated a geometric mean ^{232}Th intake of 0.40 Bq/day (gsd = 1.7 Bq/day) and geometric mean exposure time period of 1383 days for these 34 workers. However, neither urine nor serum concentration related to either the period of employment or cumulative exposure

Terry et al. (1995) assessed the fecal excretion of thorium in two workers exposed to thorium in the monazite section of a mineral sands dry separation plant over a 5-day work period followed by a 5-day work period without exposure to thorium dust. The workers had been isolated from airborne radioactive dust for at least 7 days prior to the monitoring period. For the 5-day exposure period, one worker wore an air sampler and the other a cascade impactor. Exposures totaled 26.4 Bq of 14 μm AMAD dust particles. For both workers, peak thorium fecal excretion occurred on day 6 (the day after the end of the 5-day exposure period). The rapid excretion following exposure indicated that fecal sampling can be used to assess acute exposures to thorium. During the 10-day monitoring period, fecal excretion was 970 μg thorium for one worker and 1980 μg thorium for the other worker. The 2-fold difference was unexpected and speculated to be due to mouth vs. nose breathing.

Jaiswal et al. (2004) measured thorium activity in the lungs, total body, and daily urine of 5 workers employed for 10–32 years in a plant that processed thorium hydroxide concentrate and exposed primarily by the inhalation route. The lung activity measured for each individual (15 to 67 Bq) was used to estimate their total body content and daily urine excretion. Those values were compared with measured total body content (<52 to 168 Bq) and daily urinary activity (0.46 to 1.84 mBq). Measured and calculated results compared more favorably when using the combined ICRP human respiratory tract model (ICRP 1994b) and ICRP biokinetic model (ICRP 1995) than with the older biokinetic model (ICRP 1979).

2.3.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PB) Models

The ICRP developed a Human Respiratory Tract Model (HRTM) for Radiological

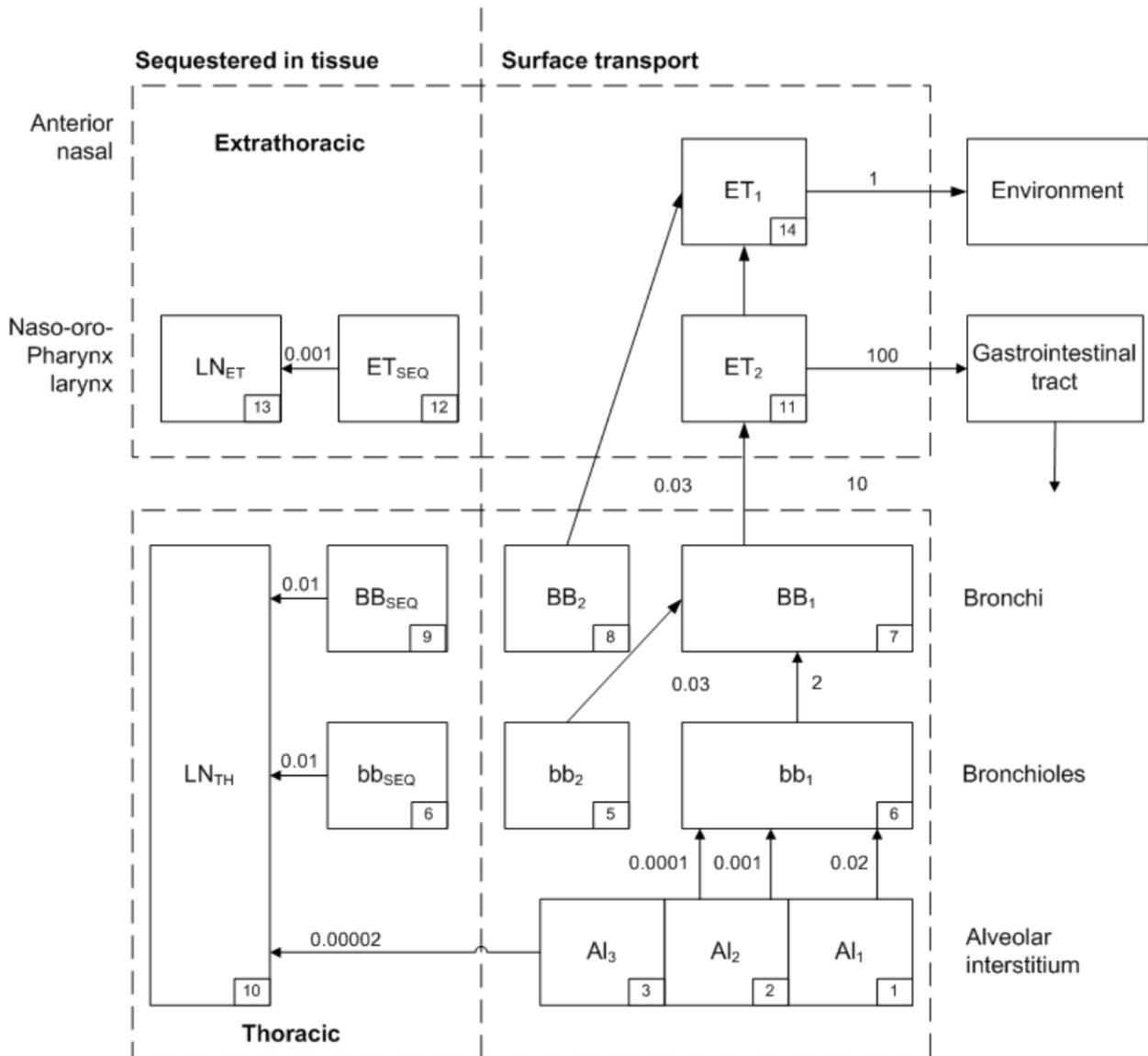
Protection, which contains respiratory tract deposition and clearance compartmental models for inhalation exposure that may be applied to thorium (ICRP 1994b; 1996). The ICRP also developed a biokinetic model for human oral exposure that applies to thorium (ICRP 1995). Several more recent enhancements to the oral exposure model have been reported. A multicompartimental gastrointestinal tract model was developed to replace what was originally a single parameter model (Human Alimentary Tract Model, HATM) (ICRP 2006). A hair compartment was developed to support biomonitoring of ingestion intakes (e.g., drinking water exposures) (WB Li et al. 2009). Drinking water and dietary exposure models and Bayesian approaches have been developed to improve thorium dose assessments made with the ICRP model (Little et al. 2003; Little et al. 2007). The NCRP has also developed a respiratory tract and biokinetics model for inhaled radionuclides (NCRP 1997).

Human Respiratory Tract Model for Radiological Protection (ICRP 1994a; 1996)

Deposition. The ICRP has developed a deposition model for behavior of aerosols and vapors in the respiratory tract. It was developed to estimate the fractions of radioactivity in breathing air that are deposited in each anatomical region. ICRP provides inhalation dose coefficients that can be used to estimate the committed equivalent and effective doses to organs and tissues throughout the body based on a unit intake of radioactive material. The model applies to three levels of particle solubility, a wide range of particle sizes (approximately 0.0005–100 μm in diameter), and parameter values can be adjusted for various segments of the population (e.g., sex, age, level of physical exertion). This model also allows one to evaluate the bounds of uncertainty in deposition estimates. Uncertainties arise from natural biological variability among individuals and the need to interpret some experimental evidence that remains inconclusive. It is applicable to particles containing uranium, but was developed for a wide variety of radionuclides and their chemical forms.

The ICRP deposition model estimates the amount of inhaled material that initially enters each compartment (see Figure 2-4). The model was developed with five compartments: (1) the anterior nasal passages (ET1); (2) all other extrathoracic airways (ET2) (posterior nasal passages, the nasopharynx and oropharynx, and the larynx); (3) the bronchi (BB); (4) the bronchioles (bb); and (5) the alveolar interstitium (AI). Particles deposited in each of the regions may be removed from each region and redistributed either upward into the respiratory tree or to the lymphatic system and blood by different particle removal mechanisms.

Figure 2-4. Respiratory Tract Compartments in Which Particles May be Deposited*



*Compartment numbers shown in lower right corners are used to define clearance pathways. The clearance rates, half-lives, and fractions by compartment, as well as the compartment abbreviations are presented in Table 2-6. Source: ICRP 1994a

For extrathoracic deposition, the model uses experimental data, where deposition is related to particle size and airflow parameters, and scales deposition for women and children from adult male data. Similarly to the extrathoracic region, experimental data served as the basis for lung (bronchi, bronchioles, and alveoli) aerosol transport and deposition. A theoretical model of gas transport and particle deposition was used to interpret data and to predict deposition for compartments and subpopulations other than adult males. Table 2-5 provides reference respiratory values for the general Caucasian population under several levels of activity.

Respiratory Tract Clearance. This portion of the model identifies the principal clearance pathways within the respiratory tract. The model was developed to predict the retention of various radioactive materials. Figure 2-5 presents the compartmental model and is linked to the deposition model (Figure 3-4) and to reference values presented in Table 2-6. Table 2-6 provides clearance rates and deposition fractions for each compartment for insoluble particles. The table provides rates of insoluble particle transport for each of the compartments, expressed as a fraction per day and also as half-time. ICRP also developed modifying factors for some of the parameters, such as age, smoking, and disease status. Parameters of the clearance model are based on human evidence for the most part, although particle retention in airway walls is based on experimental data from animal experiments.

The clearance of particles from the respiratory tract is a dynamic process. The rate of clearance generally changes with time from each region and by each route. Following deposition of large numbers of particles (acute exposure), transport rates change as particles are cleared from the various regions. Physical and chemical properties of deposited material determine the rate of dissolution and as particles dissolve, absorption rates tend to change over time. By creating a model with compartments of different clearance rates within each region (e.g., BB1, BB2, BBseq), the ICRP model overcomes problems associated with time-dependent functions. Each compartment clears to other compartments by constant rates for each pathway.

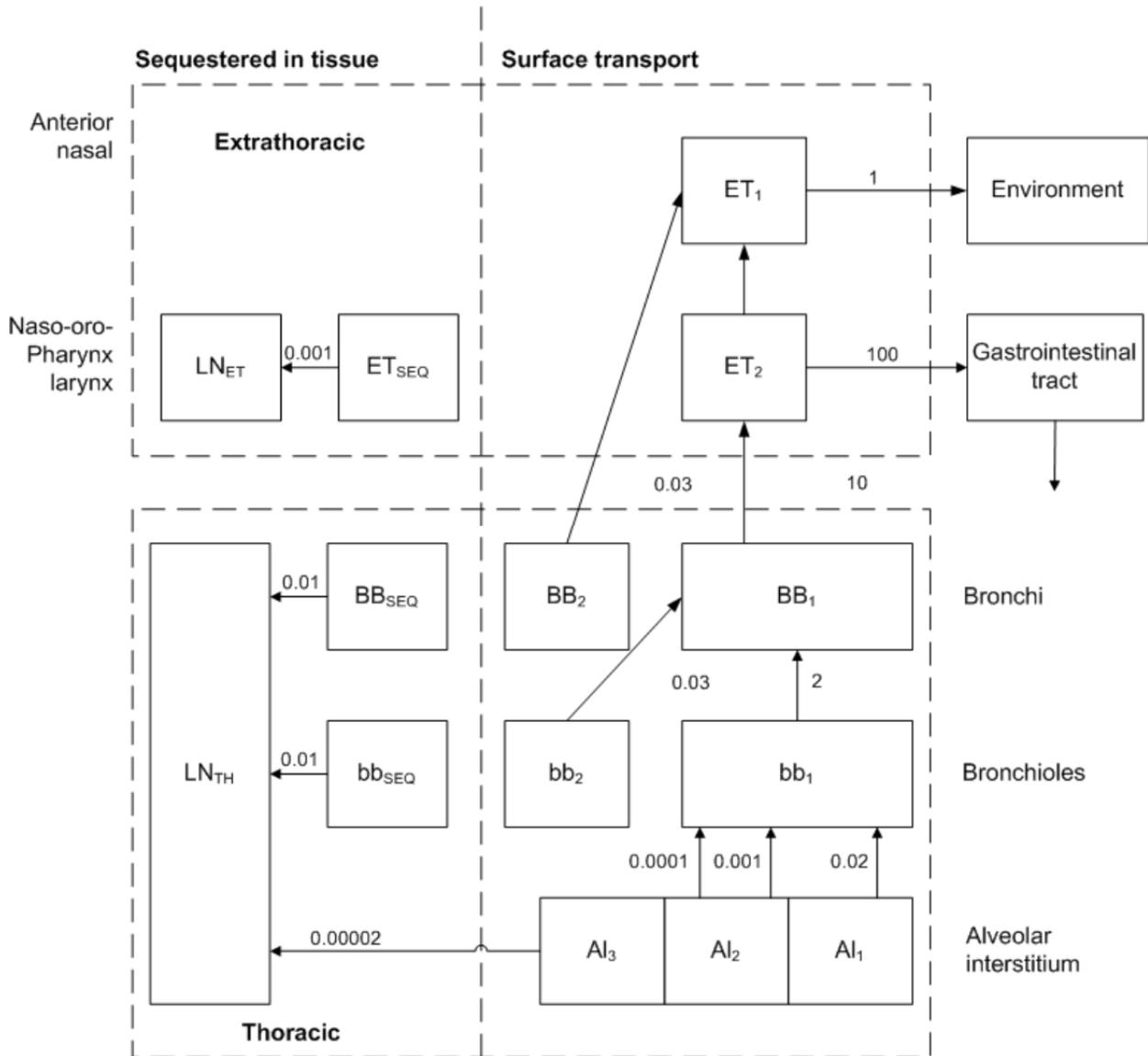
Table 2-5. Reference Respiratory Values for a General Caucasian Population at Different Levels of Activity

Breathing parameters:	3 Months	1 Year	5 Years	10 Years			15 Years		Adult	
				Male	Female	Both	Male	Female	Male	Female
Resting (sleeping); maximal workload 8%										
Breathing parameters:										
V_T (L)	0.04	0.07	0.17	–	–	0.3	0.500	0.417	0.625	0.444
B (m^3hour^{-1})	0.09	0.15	0.24	–	–	0.31	0.42	0.35	0.45	0.32
f_R ($minute^{-1}$)	38	34	23	–	–	17	14	14	12	12
Sitting awake; maximal workload 12%										
Breathing parameters:										
V_T (L)	NA	0.1	0.21	–	–	0.33	0.533	0.417	0.750	0.464
B (m^3hour^{-1})	NA	0.22	0.32	–	–	0.38	0.48	0.40	0.54	0.39
f_R ($minute^{-1}$)	NA	36	25	–	–	19	15	16	12	14
Light exercise; maximal workload 32%										
Breathing parameters:										
V_T (L)	0.07	0.13	0.24	–	–	0.58	1.0	0.903	1.25	0.992
B (m^3hour^{-1})	0.19	0.35	0.57	–	–	1.12	1.38	1.30	1.5	1.25
f_R ($minute^{-1}$)	48	46	39	–	–	32	23	24	20	21
Heavy exercise; maximal workload 64%										
Breathing parameters:										
V_T (L)	NA	NA	NA	0.841	0.667	–	1.352	1.127	1.923	1.364
B (m^3hour^{-1})	NA	NA	NA	2.22	1.84	–	2.92	2.57	3.0	2.7
f_R ($minute^{-1}$)	NA	NA	NA	44	46	–	36	38	26	33

B = ventilation rate; f_R = respiration frequency; NA = not applicable; V_T = tidal volume

Source: See Annex B (ICRP 1994b) for data from which these reference values were derived.

Figure 2-5. Environmental Pathways for Potential Human Health Effects from Thorium



See Table 2-6 for rates, half-lives, and fractions by compartment.
Source: ICRP 1994a

Table 2-6. Reference Values of Parameters for the Compartment Model to Represent Time-dependent Particle Transport from the Human Respiratory Tract

Part A

Clearance rates for insoluble particles				
Pathway	From	To	Rate (d ⁻¹)	Half-life ^a
m _{1,4}	Al ₁	bb ₁	0.02	35 days
m _{2,4}	Al ₂	bb ₁	0.001	700 days
m _{3,4}	Al ₃	bb ₁	1x10 ⁻⁴	7,000 days
m _{3,10}	Al ₃	LN _{TH}	2x10 ⁻⁵	No data
m _{4,7}	bb ₁	BB ₁	2	8 hours
m _{5,7}	bb ₂	BB ₁	0.03	23 days
m _{6,10}	bb _{seq}	LN _{TH}	0.01	70 days
m _{7,11}	BB ₁	ET ₂	10	100 minutes
m _{8,11}	BB ₂	ET ₂	0.03	23 days
m _{9,10}	BB _{seq}	LN _{TH}	0.01	70 days
m _{11,15}	ET ₂	GI tract	100	10 minutes
m _{12,13}	ET _{seq}	LN _{ET}	0.001	700 days
m _{14,16}	ET ₁	Environment	1	17 hours

Table 2-6. Reference Values of Parameters for the Compartment Model to Represent Time-dependent Particle Transport from the Human Respiratory Tract

Part B

Partition of deposit in each region between compartments ^b		
Region or deposition site	Compartment	Fraction of deposit in region assigned to compartment ^c
ET ₂	ET ₂	0.9995
	ET _{seq}	0.0005
BB	BB ₁	0.993-f _s
	BB ₂	f _s
	BB _{seq}	0.007
bb	bb ₁	0.993-f _s
	bb ₂	f _s
	bb _{seq}	0.007
Al	Al ₁	0.3
	Al ₂	0.6
	Al ₃	0.1

^aThe half-lives are approximate since the reference values are specified for the particle transport rates and are rounded in units of days⁻¹. A half-life is not given for the transport rate from Al₃ to LN_{TH}, since this rate was chosen to direct the required amount of material to the lymph nodes. The clearance half-life of compartment Al₃ is determined by the sum of the clearance rates.

^bSee paragraph 181, Chapter 5 (ICRP 1994b) for default values used for relating f_s to d_{ae}.

^cIt is assumed that f_s is size-dependent. For modeling purposes, f_s is taken to be:

$$f_s = 0.5 \text{ for } d_{ae} \leq 2.5\sqrt{\rho/\chi} \mu\text{m and}$$

$$f_s = 0.5e^{0.63(d_{ae}\sqrt{\rho/\chi}-2.5)} \text{ for } d_{ae} > 2.5\sqrt{\rho/\chi} \mu\text{m}$$

where

f _s	=	fraction subject to slow clearance
d _{ae}	=	aerodynamic particle diameter/(μm)
ρ	=	particle density (g/cm ³)
χ	=	particle shape factor

Al = alveolar-interstitial region; BB = bronchial region; bb = bronchiolar region; BB_{seq} = compartment representing prolonged retention in airway walls of small fraction of particles deposited in the bronchial region; bb_{seq} = compartment representing prolonged retention in airway walls of small fraction of particles deposited in the bronchiolar region; ET = extrathoracic region; ET_{seq} = compartment representing prolonged retention in airway tissue of small fraction of particles deposited in the nasal passages; GI = gastrointestinal; LN_{ET} = lymphatics and lymph nodes that drain the extrathoracic region; LN_{TH} = lymphatics and lymph nodes that drain the thoracic region

Source: ICRP 1994

Particle transport from all regions is toward both the lymph nodes and the pharynx, and a majority of deposited particles end up being swallowed. In the front part of the nasal passages (ET1), nose blowing, sneezing, and wiping remove most of the deposited particles. Particles remain here for about a day. For particles with AMADs a few micrometers or greater, the ET1 compartment is probably the largest deposition site. A majority of particles deposited at the back of the nasal passages and in the larynx (ET2) are removed quickly by the fluids that cover the airways. In this region particle clearance is completed within 15 minutes.

Ciliary action removes deposited particles from both the bronchi and bronchioles. Though it is generally thought that mucociliary action rapidly transports most particles deposited here toward the pharynx, a fraction of these particles are cleared more slowly. Evidence for this is found in human studies. For humans, retention of particles deposited in the lungs (BB and bb) is apparently biphasic. The “slow” action of the cilia may remove as many as half of the bronchi- and bronchiole-deposited particles. In human bronchi and bronchiole regions, mucus moves more slowly the closer to the alveoli it is. For the faster compartment, it has been estimated that it takes about 2 days for particles to travel from the bronchioles to the bronchi and 10 days from the bronchi to the pharynx. The second (slower) compartment is assumed to have approximately equal fractions deposited between BB2 and bb2 and both with clearance half-times estimated at 20 days. Particle size is a primary determinant of the fraction deposited in this slow thoracic compartment. A small fraction of particles deposited in the BB and bb regions is retained in the airway wall for even longer periods (BBseq and bbseq).

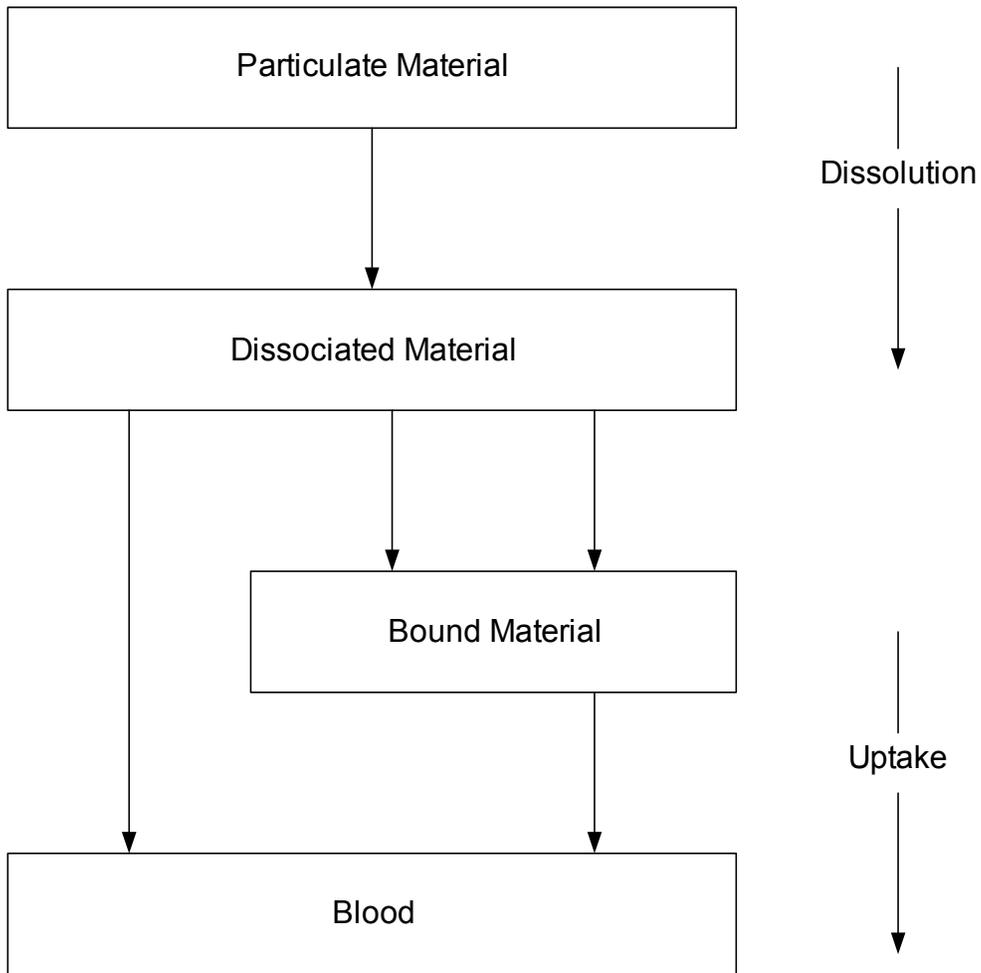
If particles reach and become deposited in the alveoli, they tend to stay imbedded in the fluid on the alveolar surface or move into the lymph nodes. The one mechanism by which particles are physically resuspended and removed from the AI region is coughing. For modeling purposes, the AI region is divided into three subcompartments to represent different clearance rates, all of which are slow. In the alveolar-interstitial region, human lung clearance has been measured. The ICRP model uses 2 halftimes to represent clearance: about 30% of the particles have a 30-day half-time and the remaining 70% are given a half-time of several hundred days. Over time, AI particle transport falls and some compounds have been found in lungs 10–50 years after exposure.

Absorption into Blood. The ICRP model assumes that absorption into blood occurs at equivalent rates in all parts of the respiratory tract, except in the anterior nasal passages (ET1), where no absorption occurs. It is essentially a two-stage process, as shown in Figure 2-6. First, there is a dissociation (dissolution) of particles; then the dissolved molecules or ions diffuse across capillary walls and are taken up by the

blood. Immediately following dissolution, rapid absorption is observed. For some elements, rapid absorption does not occur because of binding to respiratory-tract components. In the absence of specific data for specific compounds, the model uses the following default absorption rate values for those specific compounds that are classified as Types F (fast), M (medium), and S (slow):

- For Type F, there is rapid 100% absorption within 10 minutes of the material deposited in the BB, bb, and AI regions, and 50% of material deposited in ET2. Thus, for nose breathing, there is rapid absorption of approximately 25% of the deposit in ET and 50% for mouth breathing. No thorium compounds are assigned as type F; however, thorium nitrate might behave in this manner under some circumstances.
- For Type M, about 70% of the deposit in AI reaches the blood eventually. There is rapid absorption of about 10% of the deposit in BB and bb, and 5% of material deposited in ET2. Thus, there is rapid absorption of approximately 2.5% of the deposit in ET for nose breathing, and 5% for mouth breathing. Type M thorium compounds include nitrate and all other compounds than oxides, and hydroxides.
- For Type S, 0.1% is absorbed within 10 minutes and 99.9% is absorbed within 7,000 days, so there is little absorption from ET, BB, or bb, and about 10% of the deposit in AI reaches the blood eventually. Type S thorium compounds include oxides and hydroxides.

Figure 2-6. The Human Respiratory Tract Model: Absorption into Blood



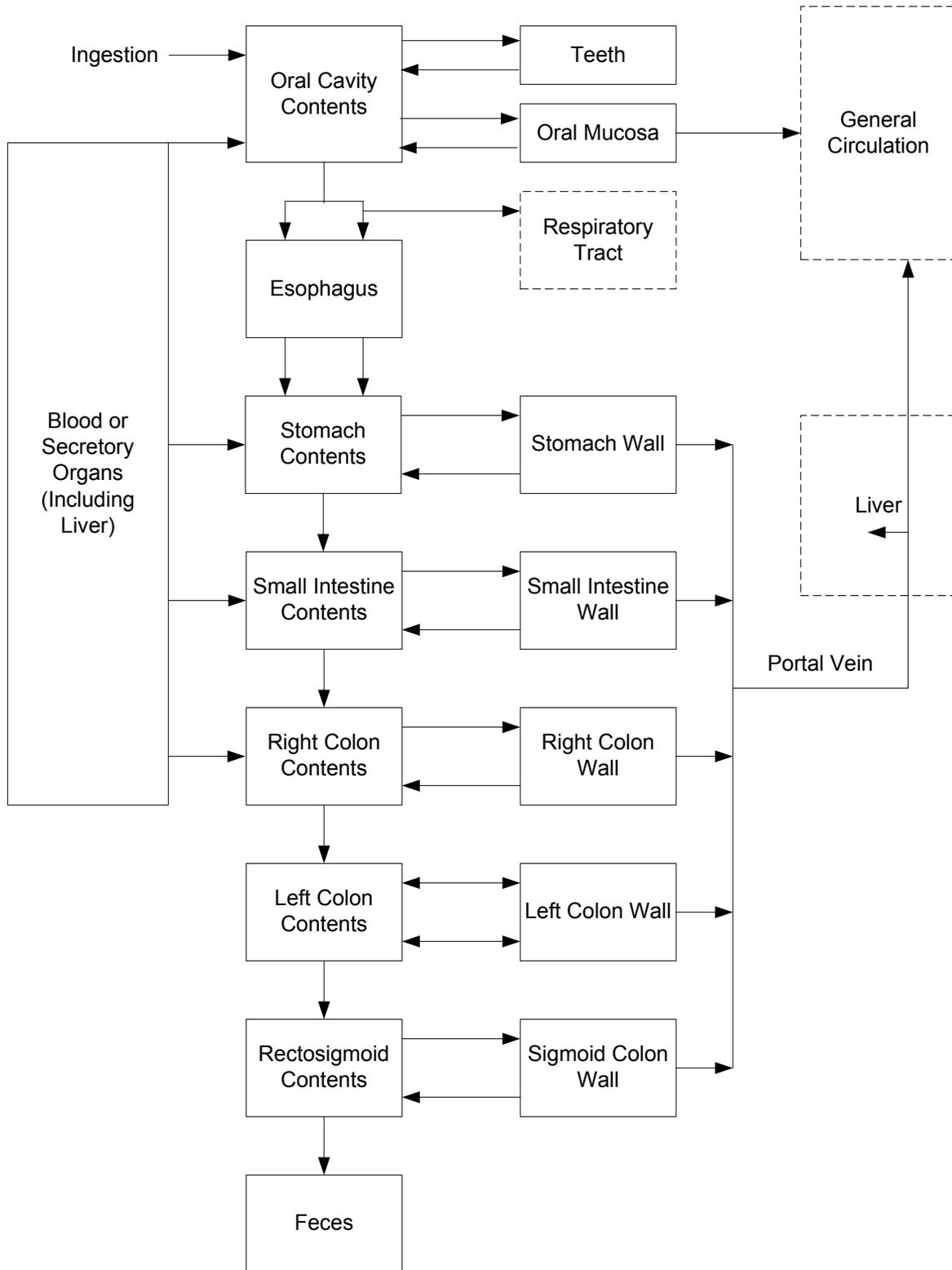
Source: ICRP 1994b

Human Alimentary Tract Model for Radiological Protection (ICRP 2006)

The ICRP HATM is a generic multicompartment gastrointestinal tract model that was developed for applications to radiation risk assessments of radionuclides. The model replaced an earlier gastrointestinal absorption model that consisted of single compartment and single parameter representation of absorption of radionuclides into the central plasma compartment from the small intestine. The structure of the multicompartment model is shown in Figure 2-7. The model simulates the following major processes that can contribute to absorption of radionuclides from the gastrointestinal tract as well as contact and retention of radionuclides in the gastrointestinal tract tissues (i.e., which could contribute to radiation dose to these tissues):

- Entry of a radionuclide into the mouth by ingestion, or into the esophagus after mechanical clearance from the respiratory tract; sequential transfer of the radionuclide through the contents of the oral cavity, esophagus, stomach, small intestine, and segments of the colon, followed by excretion in feces.
- Deposition and retention on or between the teeth and return to the oral cavity.
- Deposition and retention in the oral mucosa or walls of the stomach and intestines.
- Transfer from the oral mucosa or walls of the stomach and intestines back into the luminal contents or into blood (absorption).
- Transfer from various secretory organs or blood into the contents of certain segments of the alimentary tract (secretion).

Figure 2-7. Structure of the Human Alimentary Tract Model (HATM)



ICRP (1995) developed a compartmental model of the kinetics of ingested thorium in humans that is directly applicable to adults and contains conservative assumptions for applicability to 3 month old infants; 1, 5, and 10 year old children, and 15 year old adolescents. The model is a revision of an earlier ICRP biokinetic model of thorium (ICRP 1979). Thorium in blood distributes to the skeleton, liver, kidneys, gonads, and GI tract. Excretion pathways included in the model are kidney to urine and feces. The model has been evaluated with human data on thorium lung retention and urinary excretion and postmortem thorium tissue levels in workers exposed to airborne thorium or members of the general population without known occupational exposure to thorium (Jaiswal et al. 2004; WB Li et al. 2007; Roth et al. 2005; Stehney 1999; Terry and Hewson 1995; Terry et al. 1995). The model has also been evaluated using measured biokinetic data from rats following intratracheal instillation of thorium compounds (Hodgson et al. 2003; Stradling et al. 2001). The model has been used to establish the radiation dose (Sv) per unit of ingested or inhaled thorium (Bq) for intake ages 3 months to adult (ICRP 1995; 2001). The dose integration period is 50 years for acute intake at age 25 years. The model is designed to calculate radiation dose coefficients (Sv/Bq) corresponding to specific inhalation or ingestion exposures to thorium isotopes. Dose coefficients have been estimated for all major organs, including the bone surfaces, bone marrow, and liver, and other tissues (ICRP 1995; 1996). The model is based on both human and animal data for thorium; however, it might not reflect the distribution of injected Thorotrast due to its colloidal chemistry. However, it is intended for applications to human dosimetry. Applications to other species would require consideration of species-specific adjustments in model parameters.

2.4 RELEVANCE TO PUBLIC HEALTH

Two biokinetic models for thorium and other radionuclides have been combined to derive radiation dose coefficients from uptake via wounds, whether the material is injected or absorbed. The models are the NCRP Wound Model that describes radionuclide retention and the ICRP element-specific systemic models for radionuclide-related radiation doses. These dose coefficients are actually calculated effective doses (E_{50}) with units of Sv/Bq that can be used in conjunction with estimates of incorporated activity to estimate the 50-year effective dose to an individual. This information is useful to facilitate compliance with public and worker regulatory limits, or to indicate when medical interventions to remove activity should be considered (Toohey et al. 2011). The respective dose coefficients for ^{228}Th , ^{230}Th , and ^{232}Th are 1.18×10^{-4} , 4.19×10^{-4} , and an average 4.53×10^{-4} Sv/Bq.

Genotoxic Effects. A mixture of thorium and lanthanum in the ratio found in Brazilian monazite sand was evaluated *in vitro* for cytotoxicity and genotoxicity to human T-lymphocyte leukemia cells. The

mixture was found to be cytotoxic but not genotoxic (Oliveira et al. 2014), as described in Section 2.6 below.

Minimal Risk Levels

No changes in MRLs from October 1990 Toxicological Profile for Thorium

2.6 INTERACTION WITH OTHER CHEMICALS.

Chromosomal aberrations have been reported in the lymphocytes of occupationally exposed workers and in *in vitro* studies (ATSDR 1990). Oliveira et al. (2014) conducted *in vitro* analyses to evaluate whether occupational exposure to the multiple metals in monazite sand might result in lymphocyte toxicity (cell viability, cell death, and DNA damage). The metals included thorium, cerium, or lanthanum, either individually or combined, with combinations in ratios typically found in monazite sand. Thorium and cerium individually and Th+Ce+La did not cause toxicity in human T-lymphocyte leukemia cells during a 48 hr study. However, a >19% decrease in cell viability was observed for Th+La mixtures (≥ 0.29 mM Th + ≥ 1.17 mM La at 24 hr or ≥ 1.56 mM Th + ≥ 0.39 mM La at 48 hr). The Th+La mixtures decreased the frequency of apoptotic cells and increased the incidence of necrosis, but did not change the DNA strand break profile, indicating that this mixture is cytotoxic.

Spiethoff et al. (1992) demonstrated a pronounced interactive effect of inhaled quartz aerosols and intravenously-injected Thorotrast (colloidal $^{232}\text{ThO}_2$) on the induction of lung tumors in rats. Groups of female Wistar rats (82–87 per group) were exposed nose-only to quartz aerosols (MMAD = 1.8 μm , gsd = 2.0) at 0, 6, or 30 mg/m^3 6 hours/day, 5 days/week for 29 days followed by intravenous injection (0 or 2.96 kBq/mL) of Thorotrast. Interim sacrifices were performed at 6, 12, and 24 months post-treatment. Lifetime incidences of lung tumors in the 0, 6, and 30 mg/m^3 quartz aerosol-only exposure groups were 0/85, 37/82, and 43/82, respectively. Lung tumor incidences in those rats receiving quartz aerosol exposures at 6 or 30 mg/m^3 followed by Thorotrast injection were 39/87 and 57/87, respectively. Thorotrast treatment only resulted in 3/87 incidences of lung tumors. Whereas, lung tumor incidences in rats receiving quartz aerosol only exposure were similar to incidences in rats exposed to quartz aerosols followed by Thorotrast injection, the combined treatment resulted in marked shortening of time-to-tumor. The first lung tumor following combined treatment was detected at 1 year following treatment. The first lung tumor following quartz aerosol only exposure was detected at 17 months. By 24 months following treatment, 95 incidences of lung tumors had been identified, nearly 80% of which were detected in those

rats receiving the combined treatment. The study authors noted that lung tumor risk after 24 months was 3-fold greater in the quartz aerosol exposed and Thorotrast injected rats compared to quartz aerosol only exposed rats. The study authors suggested a possible synergistic effect with the high linear energy transfer (LET) radiation of thoron serving as an initiator and quartz acting as a promoter.

2.9 METHODS FOR REDUCING TOXICITY.

2.9.2 Reducing Body Burden

H Chen et al. (2005) injected mice intraperitoneally with 0.6 MBq of ^{232}Th in 1% sodium citrate and, after a period of 3 minutes or 3 days, intramuscularly injected 4 ligands to assess decorporation effectiveness. Those included vitamin E, DTPA (CaNa_3 -diethylenetriaminepentaacetic acid), and 2 specially prepared catecholicpolyaminopolycarboxylate-derived compounds (#7,601, catechol-3,6-bis-methyleneiminodiacetic acid, and #9,501, 3,3-methylene iminoethylene N,N-diaceticacid dicatechol). Prompt administration of #7,601, #9,501, or DTPA respectively reduced Th in the body by 86, 82, and 72%, in bone by 17, 6, and 50%, and in liver by 6, 13, and 8%. Four days after exposure, the morphology of bone marrow tissue was unchanged in the #7,601 and #9,501 treated mice, capillaries were dilated in the DTPA group, and clear radiation damage was observed in controls or untreated animals.

Kumar et al. (2012) injected rats i.m. with 0.6 mg/kg thorium as thorium nitrate, and after 6 h, with 11.2 mg DTPA/kg as plain DTPA or DTPA encapsulated in uncharged liposomes. They reported that liposomal encapsulation enabled DTPA to reach higher concentrations in liver and blood, and to be retained longer. Encapsulated DTPA was approximately twice as effective as DTPA alone at decorporating thorium. In liver, the % of injected thorium was reduced from 42% to 33% by DTPA and to 22% by encapsulated DTPA. Similar results were reported for blood, for which values were approximately a quarter of those for liver.

(Yantasee et al. 2010) evaluated the potential for direct decorporation of thorium from blood and plasma by flowing blood over a monolayer of test chelators attached to a high surface area mesoporous silica substrate. This method has the potential for accomplishing decorporation outside the body (comparable to dialysis) without the side effects associated with internal chelation. The hydroxypyridinone isomer, 3,4-HOPO, was more effective than DTPA at chelating thorium (as well as plutonium, americium, and uranium), achieved a 50% reduction in thorium blood concentration within minutes, and remained attached to the substrate.

2.9.3 Interfering with the Mechanisms of Action

H Chen et al. (2005) reported that catecholicpolyaminopolycarboxylate compounds #7,601 and #9,501 exhibited anti-oxidant action by reducing both cell killing in the bone marrow and malondialdehyde levels (a measure of lipid peroxidation) in bone marrow and liver.

Shiga et al. (1993) reported that administration of the antitumor drug PSK (Polysaccharide Kureha, a protein-bound polysaccharide extracted from basidiomycete fungi) resulted in decreased incidences of hepatic tumors (from 22.5% to 10.5%) in Syrian hamsters injected with 0.09 g of Th as Thorotrast. The incidence rate in controls was 2.8%.

3. CHEMICAL AND PHYSICAL INFORMATION

3.2 PHYSICAL AND CHEMICAL PROPERTIES

When the solubility of a low solubility thorium compound is different than expected or reported, the cause could be changes in surface form due to external factors, such as high temperature. Vandenborre et al. (2010) scanned the surface of sintered thorium oxide using x-ray photoelectron spectroscopy (XPS) and found it to consist of 2 forms, 80% ThO_2 and 20% $\text{ThO}_x(\text{OH})_y(\text{H}_2\text{O})_z$, which have different solubilities. The rate of surface detachment for this oxide was measured, then ^{239}Th was added and the surface attachment rate determined. The net balance disagreed with the thermodynamic calculation for pure ThO_2 .

Table 3-2. Physical and Chemical Properties of Thorium and Compounds

Property	Thorium Chloride	Thorium Sulfate	Reference
Atomic/molecular Weight	373.849	586.303	Web_elements (2014a) Web_elements (2014b)
Chemical formula	ThCl ₄	Th(SO ₄) ₂ ·9H ₂ O	Web_elements (2014a) Web_elements (2014b)
Synonyms	Thorium tetrachloride; thorium(IV) chloride; thorium chloride	Thorium disulphate; sulfuric acid, thorium; thorium sulfate nonahydrate; thorium sulfate 9-water; thorium (IV) sulfate 9-water	Web_elements (2014a) Web_elements (2014b)
Common names	No data	No data	
CAS Registry No.	10026-08-1, 54327-76-3	10381-37-0	Web_elements (2014a) Web_elements (2014b)
Color	White to gray	White	Web_elements (2014a) Web_elements (2014b)
Physical state	Crystalline solid	Crystalline solid	Web_elements (2014a) Web_elements (2014b)
Odor	No data	No data	
Melting point, °C	770	400 (dehydrates)	Web_elements (2014a) Web_elements (2014b)
Boiling point, °C	921	NA	Web_elements (2014a) Web_elements (2014b)
Autoignition Temperature	No data	No data	
Solubility:			
Water	Soluble	4.2 g/100 g H ₂ O	Web_elements (2014a) Web_elements (2014b)
Other solvents	No data	No data	Web_elements (2014a) Web_elements (2014b)
Density g/cm ³	4.59	2.8	Web_elements (2014a) Web_elements (2014b)
Partition coefficients	No data	No data	
Vapor pressure	No data	No data	
Henry's law constant	No data	No data	
Refractive index	No data	No data	
Flashpoint	No data	No data	
Flammability limits	No data	No data	

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL

4.3 Use

Trastuzumab is a humanized monoclonal antibody approved by the Food and Drug Administration for treating metastatic breast cancer in individuals who overexpress the human epidermal growth factor receptor 2 (HER2) oncogene. Heyerdahl et al. (2012) evaluated the relative efficacy of subcutaneously-injected single dose (1 MBq/kg) versus fractionated dose (4 x 0.25 MBq/kg) therapy with ^{227}Th -DOTA-p-benzyl-trastuzumab (^{227}Th -trastuzumab) for cancer treatment in nude mice. Fractionating the dose of ^{227}Th -trastuzumab reduced toxicity while maintaining therapeutic value, indicating that fractionation might allow for increased treatment doses aimed at improving cancer therapy. Heyerdahl et al. (2011) also found that ^{227}Th -trastuzumab at clinically relevant concentrations inhibited cell growth, decreased cell survival, and increased apoptosis in human breast cancer cell lines (BT-474 and SKBR-3) as well as in an ovarian cancer cell line (SKOV-3) in a dose-dependent manner.

^{227}Th has been proposed for the palliative treatment of skeletal pain associated with cancers metastasized from other organs so as to improve the quality of life. ^{227}Th deposits on bone surfaces based on its chemical properties independent of its radiological properties and radioactive progeny. Deposition sites receive 28 MeV of localized alpha energy (within micrometers of the deposition sites) over a short period of weeks resulting from its 18.7 d half-life and rapidly-approached secular equilibrium with its alpha-emitting progeny. Ogawa and Washiyama (2012) suggested that bonding ^{227}Th to ethylenediaminetetramethylenephosphonic acid (EDTPM) should enhance the efficacy of pain treatment since the complex increases the skeletal deposition and retention of thorium and its progeny. It also speeds excretion from soft tissue and blood, thus reducing radiation dose to those tissues. Similar ^{227}Th complexes involve bonding with diethylenetriaminepentamethylenephosphonic acid (DTPMP) and 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylenephosphonic acid (DOTMP).

In addition to DTPA being tested as a thorium chelator, it has been studied as a radiotherapy agent. Le Du et al. (2012) identified that DTPA could be labeled in vitro with ^{226}Th to produce a complex with thorium. When injected, the thorium would interact strongly with human serum transferrin such that the complex might be used as a delivery system in targeted alpha therapy.

In February 1976, the European Union made it illegal to commercially export African elephant raw tusk ivory. Schmied et al. (2012) determined that the ratio of $^{228/232}\text{Th}$ in the ivory can be used in conjunction with ^{14}C and ^{90}Sr dating to help confirm the time of death. One method involves removing ~10 g of ivory from the base (the area of newest growth) and analyzing the ashed, extracted, and electrodeposited sample

by alpha spectroscopy. The accuracy and relevance of this approach was validated using standard reference materials.

4.4 DISPOSAL

Akkaya (2013) synthesized a polymerized derivative of pumice (poly-hydroxyethylmethacrylate-pumice or P(HEMA-Pum)) and evaluated its effectiveness in adsorbing Th^{4+} ions from solution in order to assess its potential for decontaminating ground and surface water. A total of 0.1 g of adsorbant was agitated for 24 hours in 10 mL of thorium nitrate solution of various concentrations and pH. The adsorption process was endothermic, increased system entropy, was spontaneous, and peaked at pH 3.0. Results demonstrated that P(HEMA)Pum has the potential to adsorb up to 0.21 $\mu\text{mol Th/g}$ medium from a liquid solution. Repetitive testing and cleaning demonstrated the medium to be reusable at least 5 times.

Chandramouleeswaran et al. (2011) tested two boroaluminosilicate glasses with surface area 102 cm^2/g for their ability to adsorb thorium from a solution containing thorium nitrate with or without uranium. Such glasses are used to vitrify and immobilize high level liquid radioactive waste. The glass with the lower $\text{B}_2\text{O}_3:\text{Na}_2\text{O}$ ratio (0.23 vs. 9.8) was more effective at removing thorium. Its thorium uptake peaked at pH 7.5-8, reached saturation at 12 mg Th/g glass, and was selective against uranium.

GY Li et al. (2011) evaluated fifteen plant species for ability to bioaccumulate thorium and other metals from a uranium mill tailings repository in South China. *Phragmites australis* was found to have the greatest capability for removing uranium, thorium, barium, and lead, with respective “phytoremediation factors” of 17, 9, 10, and 10. However, none of the species were classified as hyperaccumulators for these metals.

5. POTENTIAL FOR HUMAN EXPOSURE

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

More recent studies provide support to previous findings that thorium in soil can adhere to plant roots (Shtangeeva 2010), while relatively little transfers to the upper parts and is slowly taken up by plants (SB Chen et al. 2005; Morton et al. 2002; Pulhani et al. 2005; Rayno 1989; Shtangeeva 2010; Shtangeeva et al. 2005). Baeza and Guillen (2006) reported that mushrooms remove thorium from soil, with uptake being an order of magnitude higher for *Munõveros* than *Bazagona* mushrooms. For both varieties combined, the soil-to-mushroom transfer factors (the ratio of meat to gross soil concentration) ranged from 0.030-0.62, which is comparable to factors for uranium, ^{90}Sr , ^{241}Am , and $^{239+240}\text{Pu}$. The available transfer factor (considering only that portion of the thorium in soil that is available for transfer to plants) was 2 orders of magnitude higher and ranged from 3-371 (which is comparable to factors for ^{137}Cs).

The presence of EDTA in soil (e.g., at a mill or waste disposal site) can increase the rate at which a thorium plume moves through the earth. Abdel-Fattah et al. (2013) passed mixtures of thorium (0.4–4 mM) and EDTA (4–40 mM) with Th:EDTA ratios of 1:1 to 10:1 through sand at rates of 20–100 m/yr to simulate conditions at the UK low level waste repository at Drigg. May et al. (2012) studied the migration of thorium-EDTA mixtures through sand-packed columns. Thorium migrated very slowly when EDTA was absent. Migration rate changed as functions of thorium and EDTA concentration, as well as with thorium species. The relative abundances of 10 identified thorium species depended on the thorium:EDTA concentration ratio. At low thorium concentrations, the thorium-EDTA complex was considered to interact with sand surfaces, and transport depended on groundwater flow rate. But at higher thorium concentrations, plume flow was higher than expected. This might be due to the formation of a thorium colloid associated with natural minerals and not necessarily with EDTA, as has been reported for plutonium colloids.

Ishikawa et al. (2004) observed relatively high concentrations of ^{234}Th in livers (50–400 Bq/kg dry) and excrement (2,000–2,900 Bq/kg dry) from marine ascidians, whereas parent ^{238}U concentrations were less than 3 Bq/kg dry. These findings indicate biomagnification of ^{234}Th in the liver.

The Toxicological Profile for Thorium (ATSDR 1990) noted that reported soil to plant transfer coefficients (concentration in dry plant to concentration in dry soil) were in the range of 10^{-4} to 7×10^{-3} , but

that it could be as high as 2.9 for mixed grasses under certain conditions. Jeambrun et al. (2012) conducted a study of uranium and thorium uptake in plants from 5 French areas. Soil-to-plant transfer factors were lower for ^{232}Th than ^{238}U , and those factors for ^{232}Th were lower in wheat (mean = 0.0014) than in lettuce (0.013).

Soudek et al. (2013) artificially exposed the roots of hydroponically grown tobacco plant seedlings (*N. tabacum* cv. La Burley 21) over a 16 day period to media containing thorium nitrate (50, 100, 250, or 500 μM) with various concentrations of organic acid chelators (citric, tartaric, and oxalic) or in the absence of phosphate or iron. The absence of phosphate most significantly affected thorium uptake. Levels in all plant parts increased gradually as a function of thorium concentration and extent of phosphate and iron depletion. The highest thorium dose with no phosphate resulted in thorium levels of 82 $\mu\text{g}/\text{kg}$ dry weight (DW) in roots, 6 $\mu\text{g}/\text{kg}$ DW in stems, and 1 $\mu\text{g}/\text{kg}$ DW in leaves, while the addition of 2 mM phosphate retarded thorium uptake. Effects of iron deprivation were less, while the impact of acids peaked for 0.5 mM citric or tartaric acids resulted in thorium increases in roots and stems, but not in leaves. The phosphate deficient thorium uptake factor for tobacco seedling leaves can be calculated as 0.002.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.3 Soil

Gallegos (1995) reported mean ^{232}Th levels of 0.0265, 0.0259, and 0.0351 Bq/g dry (0.716, 0.7, and 0.949 pCi/g dry) in soil samples taken from sampling sites in the vicinity of the Lawrence Livermore National Laboratory in California. Powell et al. (2007) found much higher levels in sediment samples taken from the Reedy River and surrounding creeks in Simpsonville, South Carolina that averaged 45.3 Bq/kg (1.22 pCi/g).

Hydraulic fracturing (fracking) operations to enhance natural gas production use water and additives injected under pressure and the process results in pits, ponds, and impoundments, referred to as reserve pits, on the surface. Rich and Crosby (2013) collected water and residual sludge from two reserve pits in the Barnett Shale East Newark Field and found ^{228}Th concentrations ranging from 0.36 to 0.72 pCi/g. Water concentrations were not reported.

Coal combustion residues (CCRs) from coal-fired power plants contain thorium, uranium, and a range of other substances. Spills from containment impoundments, such as the one in Kingston, TN in 2008, can adversely affect the environment, so EPA undertook evaluation of such sites. Roper et al. (2013)

analyzed samples from a 74-site subset of that larger EPA study. The concentration of ^{232}Th in fly ash averaged 73 ± 26 Bq/kg for bituminous coals and 81 ± 18 Bq/kg for subbituminous coals, 10 ± 6 Bq/kg in scrubber sludges, and 1 ± 1 Bq/kg in flue gas desulfurization gypsum.

Normally, thorium concentrations in drinking water are low and EPA does not require levels to be measured. Since thorium and other elements can become trapped in solids that deposit on sediment and walls of distribution system piping, levels can build up over time. Lytle et al. (2014) collected and analyzed samples of solids from the flushing of deposits (primarily from fire hydrants) in 25 distribution systems from 12 water utilities. Total thorium averaged 40 ± 25 pCi/g and consisted of $>90\%$ ^{228}Th (36 ± 24 pCi/g), $\sim 8\%$ ^{230}Th (3.3 ± 3.0 pCi/g), and $\sim 3\%$ ^{232}Th (1.2 ± 1.1 pCi/g). The flushing of water distribution systems can remove thorium and result in lower levels at the tap, especially if the system is otherwise undisturbed.

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

An autopsy study from the U.S. Transuranium and Uranium Registry reported that the maximum concentrations of ^{232}Th for an individual who was not occupationally exposed to thorium ranged from 20-400 ng/g in lung and 160-400 ng/g in lymph nodes (Hare et al. 2010).

Thorium concentrations in the air of an ore-crushing workshop associated with a rare-earth mine in China ranged from 9.30 to 875 mg/m^3 and averaged 188.7 mg/m^3 (Chen et al. 2003).

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Welders are exposed to elevated airborne thorium levels when using thoriated tungsten welding electrodes during the process of tungsten inert gas (TIG) welding (Gafvert et al. 2003; Ludwig et al. 1999; McElearney and Irvine 1993; Saito et al. 2003), even though the welding process is not intended to consume the electrode. Additional inhalation exposure of those welders could occur while grinding one end of each electrode to a point in preparation for its use.

Firefighters may be exposed to elevated levels of thorium when inhaling smoke from forest fires. Carvalho et al. (2014) found that the complete combustion of plants in the Viesu district of Portugal resulted in fly ash with a thorium concentration of 412 Bq/kg, which was over 100 times that of the original vegetation (range 0.023-5.5 Bq/kg).

Lenka et al. (2013) estimated the ingestion radiation doses from thorium and other environmental radionuclides in food and water to the population of Chhatrapur, Odisha, India. The area is rich in monazite sand, which contains elevated levels of uranium and thorium series radionuclides. The respective average doses from cereals, pulses, and drinking water were 50, 2.4, and 0.2 $\mu\text{Sv}/\text{yr}$. Cereals were highest due to their combined radioactivity concentration (up to 2 mBq/g) and intake rate.

6. ANALYTICAL METHODS

6.1 BIOLOGICAL MATERIALS

Inductively coupled plasma combined with mass spectrometry (ICP-MS) has been used to detect relatively low levels of ^{232}Th in urine samples without complicated sample preparation; detection limits of 0.001 Bq/L or lower were achieved depending upon the dilution factors used in the investigation (Baglan et al. 2001). Neutron activation analysis has been used to measure ^{232}Th levels in blood and urine of human subjects at levels in the ng/L (4×10^{-6} Bq/L) range (Dang et al. 1989).

6.2 ENVIRONMENTAL SAMPLES

Mola et al. (2014) developed a method to improve thorium recovery, reduce detectable activity, and increase sample throughput for environmental sludge samples. Phosphogypsum sludge with IAEA reference certification and drinking water treatment facility (DWTF) sludge samples were prepared by dry ashing, microwave digestion using EPA Method 3051A, reconstitution, and elemental separation using a new and semiautomated sequential radiochemical separation method with an extraction chromatographic resin, followed by electrodeposition. The authors reported that their microwave-extraction method compared to a standard manual method significantly increased thorium recovery ~10% (e.g., 80% to 88% for DWTF sludge) and reduced minimum detectable activity by ~50% to 85%.

Okubo et al. (2013) described a method to rapidly extract thorium from seawater. Iron and thorium were simultaneously extracted on an iron hydroxide recovery resin column then backflow eluted. The thorium was recovered on an anion exchange resin, then eluted for ICP-MS analysis. Processing for ^{232}Th analysis was reduced from ~20 hr to 3-4 hr.

Lazo et al. (1991) developed an X-ray fluorescence spectroscopic procedure which determines the levels of ^{232}Th in soil samples. Unprocessed soil samples are irradiated with γ rays obtained from a ^{57}Co source. Induced fluorescence emissions from the innermost K_{α} shell of thorium are detected using a high purity germanium planar detector and the area of the fluorescent peak is correlated to the concentration of ^{232}Th in soil.

Neutron activation analysis (NAA) is an efficient analytical method to determine the activity of ^{232}Th in different environmental matrices, particularly in difficult to dissolve samples. The use of NAA, α -spectrometry and γ -ray spectrometry to measure levels of ^{232}Th in citrus leaves, aqueous solutions, ore

and sand samples have been compared. In each case, Kuppers (2001) found that NAA was equally or more sensitive than other spectroscopic methods, especially for the sand and ore samples in which case α -spectrometry could not be used because the samples could not be dissolved.

7. REGULATIONS AND ADVISORIES

In 1981, the National Toxicology Program (NTP) classified ThO_2 as known to be a human carcinogen (NTP 2011). The International Agency for Research on Cancer (IARC) classified ^{232}Th and its decay products, administered intravenously as a colloid dispersion of ^{232}Th dioxide, as a group 1 carcinogen, i.e., carcinogenic to humans. However, IARC has not found sufficient evidence to classify as carcinogenic any other form of thorium, e.g., ThO_2 associated with mines and mills (IARC 2001).

Table 7-1. Regulations and Guidelines Applicable to Thorium

Agency	Description	Information	Reference
INTERNATIONAL GUIDELINES			
IARC	Carcinogenicity classification Thorium-232 and its decay products, administered intravenously as a colloidal dispersion of thorium-232 dioxide	Group 1 ^a	IARC (2014)
WHO	Air quality guidelines	No	WHO (2005)
	Drinking water quality guidelines	1 Bq/L ²²⁸ Th, ²³⁰ Th, or ²³² Th	WHO (2011)
NATIONAL REGULATIONS AND GUIDELINES			
a. Air			
ACGIH	TLV (8-hour TWA)	No	ACGIH (2014)
NIOSH	REL (10-hour TWA)	No	NIOSH (2014)
	IDLH	No	
OSHA	PEL (8-hour TWA) for general industry	No	OSHA (2014) 29 CFR 1910.1000, Table Z-1
b. Water			
EPA	Drinking water standards and health advisories	No	EPA (2012)
	National primary drinking water standards	No	EPA (2014)
c. Other			
ACGIH	Carcinogenicity classification	No	ACGIH 2009
	Biological exposure indices	No	
EPA	Carcinogenicity classification	No	IRIS (2014)
	RfC	No	
	RfD	No	
NTP	Carcinogenicity classification Thorium dioxide	Known to be a human carcinogen ^b	(NTP (2011))

^aGroup 1: carcinogenic to humans.

^bBased on sufficient evidence of carcinogenicity in humans.

ACGIH = American Conference of Governmental Industrial Hygienists; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; STEL = short term exposure limit; TLV = threshold limit values; TWA = time-weighted average; WHO = World Health Organization

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9. GLOSSARY

No updated data