U.S. Department of Energy
Livermore Field Office, Livermore, California 94551

Lawrence Livermore National Laboratory
Lawrence Livermore National Security, LLC, Livermore, California 94551

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Mammalian and Avian Toxicity Reference Values for use in the Building 812 Baseline Ecological Risk Assessment at Lawrence Livermore National Laboratory Site 300

Author:

T. Carlsen

April 2013

Environmental Restoration Department

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Executive Summary

A baseline ecological risk assessment (BERA) is being conducted for the Building 812 Operable Unit, Lawrence Livermore National Laboratory Site 300, by the United States Department of Energy (DOE) and Lawrence Livermore National Laboratory (LLNL). A baseline risk assessment work plan (BRAWP) was prepared by DOE/LLNL and approved by the United States Environmental Protection Agency (EPA), the California Department of Toxic Substance Control (DTSC) and the California Central Valley Regional Water Quality Control Board (RWQCB) (collectively known as the regulatory agencies) in January 2012 (Carlsen et al., 2012). As described in the BRAWP, the deer mouse (*Peromyscus maniculatus*) and the rock wren (*Salpinctes obsoletus*) were selected as representative species for the Building 812 BERA (Section 3.1.6 of the BRAWP). As described in Sections 3.3.4.3 and 3.3.4.4 of the BRAWP, modeling will be conducted to evaluate rock wren and deer mouse exposure to uranium and other heavy metals in surface and subsurface soil.

In order to conduct the deer mouse and rock wren exposure modeling, mammalian and avian toxicity reference values (TRVs) are required for the preliminary contaminants of ecological concern (PCOECs). The PCOECs identified in the BRAWP are copper, lead, nickel, zinc and uranium. As described in Sections 3.3.4.3 and 3.3.4.4 of the BRAWP, the avian and mammalian TRVs for copper, lead, nickel and zinc are those developed by the United States Environmental Protection Agency (EPA) during the development of the ecological soil screening levels (Eco-SSLs) for these metals (U.S. EPA, 2005; U. S. EPA, 2007a, b and c). The TRVs for these metals are shown in Table EX-1.

Mammalian and avian TRVs for uranium have not been developed by the EPA. The TRVs used in the Building 812 screening-level ecological risk assessment (SLERA) were based on those developed by Sheppard et al. (2005) and Sample et al. (1996). For the BERA, the BRAWP calls for the development of a mammalian and avian TRV for uranium following the standard operating procedures (SOPs) developed by the EPA for use in the development of Eco-SSLs as closely as possible (U.S. EPA, 2003a,b; U. S. EPA, 2007d,e). These SOPs require an extensive literature search; review and coding of identified abstracts; review of all retrieved literature and extraction of toxicity data; and analysis of the toxicity data using a weight-of-evidence approach for the derivation of the TRV.

Almost 300 citations and associated abstracts were reviewed for relevance in developing a mammalian TRV for uranium. From this review, 128 papers were obtained and reviewed, from which toxicity information was extracted from 50 papers. From these papers, 281 individual results were extracted, of which 201 were used in the development of the mammalian TRV for uranium. Results were obtained dealing with biochemical, pathological, behavioral, mortality, growth and reproductive endpoints. Using a weight-of-evidence approach based on U. S. EPA (2007d), a mammalian TRV of 1 milligram (mg) uranium/kilogram (kg) body weight/day was developed and is shown in Table EX-1.

From the literature search, only 28 citations were identified as potentially relevant to the development of an avian TRV for uranium. Upon review of the associated abstracts, a single paper considering sub-chronic oral exposure to uranium, and a single paper on acute, non-oral exposure was identified and reviewed. These are the same two papers considered by Sheppard et al. (2005) and Sample et al. (1996) and used to develop the avian TRV used in the Building 812

SLERA. Because of the limited toxicological data available, it was not possible to derive an avian TRV following a protocol based on U.S. EPA (2007e). Therefore, the avian TRV of 10 mg uranium/kg body weight/day used in the SLERA will be used in the Building 812 BERA and is shown in Table EX-1.

Table EX-1. Toxicity Reference Values that will be used in the exposure modeling for the Building 812 baseline ecological risk assessment.

	Toxicity Reference Value (mg PCOEC/kg body wt/d)		
PCOEC	**Birds**	**Mammals**	**Source**
Copper	**4.05**	**5.60**	**USEPA 2007a**
Lead	**1.63**	**4.70**	**USEPA 2005**
Nickel	**6.71**	**75.4**	**USEPA 2007b**
Zinc	**66.1**	**75.4**	**USEPA 2007c**
Uranium	**10**	**1**	**This document**

Notes:
- **d =** **Day.**
- **mg =** **Milligram.**
- **PCOEC =** **Preliminary Contaminant of Ecological Concern.**
- **kg =** **Kilogram.**
- **wt =** **Weight.**

Introduction

A baseline ecological risk assessment (BERA) is being conducted for the Building 812 Operable Unit, Lawrence Livermore National Laboratory Site 300, by the United States Department of Energy (DOE) and Lawrence Livermore National Laboratory (LLNL). A baseline risk assessment work plan (BRAWP) was prepared by DOE/LLNL and approved by the United States Environmental Protection Agency (EPA), the California Department of Toxic Substance Control (DTSC) and the California Central Valley Regional Water Quality Control Board (RWQCB) (collectively known as the regulatory agencies) in January 2012 (Carlsen et al., 2012). As described in the BRAWP, the deer mouse (*Peromyscus maniculatus*) and the rock wren (*Salpinctes obsoletus*) were selected as representative species for the Building 812 BERA (Section 3.1.6 of the BRAWP). As described in Sections 3.3.4.3 and 3.3.4.4 of the BRAWP, modeling will be conducted to evaluate rock wren and deer mouse exposure to uranium and other heavy metals in surface and subsurface soil.

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Literature Search

The literature search was conducted based on U.S. EPA (2003a), "*Guidance for Developing Ecological Soil Screening Levels (Eco-SSLs), Attachment 4-2, Standard Operating Procedure (SOP) #3: Wildlife Toxicity Reference Value Literature Search and Retrieval*". Although the use of Dialog was described in U. S. EPA (2003a), LLNL has site-licenses with all the relevant databases, and therefore the databases were queried directly rather than going through Dialog. In addition, an initial query using the database Agricola and NTIS revealed these databases to not provide relevant citations, and therefore were not used.

Search terms for uranium included uranium, uranium compounds, uranyl, uranic and RN=7740-61-1. Receptor search terms were those described in U.S. EPA (2003a) for avian receptors, laboratory mammals and wild mammals, and are shown in Table A-1 in Appendix A.

The following toxicological terms were used (the * denotes the term was truncated):

Search Terms	Exclusion terms
reproduce*	human*
systemic	vitro
development*	culture*
histology	inhalation
growth	subcutaneous
neurological	inject*
behave*	gene
mortal*	carcin*
lethal*	cancer*
diet	tumo*
dietary	
surviv*	
drinking water	

All retrieved citations were downloaded into an Excel spreadsheet, and associated abstracts were downloaded into a Word document. All citations and associated abstracts were reviewed and coded as described in Section 2 "*Review of Literature and Rejection Criteria*" of U.S. EPA (2007d), "*Guidance for Developing Ecological Soil Screening Levels (Eco-SSLs), Attachment 4-3, Standard Operating Procedure (SOP) #4: Wildlife Toxicity Reference Value Literature Review, Data Extraction and Coding*". Rejection codes used from U.S. EPA (2007d) are shown in Table A-2. Full papers from citations passing the first screen were obtained and further reviewed for applicability and additional papers were subsequently rejected as not applicable for use in the TRV development. Potentially relevant papers cited in reviewed papers were also obtained and reviewed for applicability. Table A-3 shows those papers rejected from the mammalian TRV development and Table A-4 shows those papers rejected for use in the avian TRV development.

Toxicity data from retained papers was extracted and coded as described in Section 4 of U.S. EPA (2007d). Results of all endpoints from each unique phase or experiment were entered into an Excel spreadsheet with a column for each record identified in U.S. EPA (2007d). As discussed in U.S. EPA (2007d), a phase was considered unique if it used a different form of uranium, different receptor species or different exposure lengths. Results for males and females were generally not scored as separate phases. If the results for the two sexes differed, the most conservative [i.e. lowest No Observable Adverse Effect Level (NOAEL) or Lowest Observable Adverse Effect Level (LOAEL)] was scored, and the higher result noted in the NOAEL/LOAEL

Comments column]. Endpoints were identified by major effect group (biochemistry, pathology, behavior, growth, reproduction and mortality), and were further described by an effect type and an effect measure. Table A-5 lists the effect groups, effect types and effect measures from U.S. EPA (2007d) used in the uranium toxicity literature data extraction. Instead of describing the response site, as called for in U.S. EPA (2007d), this column was renamed "Endpoint Description" which allowed for a finer description of the endpoint studied.

Each result was then evaluated and scored based on the scoring system described in U.S. EPA (2003b), "*Guidance for Developing Ecological Soil Screening Levels (Eco-SSLs), Attachment 4-4, Standard Operating Procedure (SOP) #5: Wildlife TRV Data Evaluation"*. The scoring system assigns a score ranging from zero (no merit in setting a TRV) to 10 (extremely valuable and relevant to setting a TRV) to each of 10 toxicological study attributes. The ten attributes are data source, chemical form, test concentration, dose quantification, dose range, dose route, endpoint, exposure duration, statistical analysis and test conditions. A description of each toxicological attribute and scoring values used for evaluating the uranium toxicological literature is given in Table A-6. Statistical power, as described in U.S. EPA (2003b), was not explicitly calculated for each result. Rather, points were given for the category Statistical Analysis based on the whether an acceptable statistical analysis was conducted and adequately described. In addition, under the attribute Dose Range, reported NOAEL-only values were given a score of 5, where as LOAEL-only values were given a score of 4. U.S. EPA (2003b) scored both equally at 4.

A value of 60 was used as the minimum value required for a result to be used in the derivation of a TRV, rather than the value of 65 used in U.S. EPA (2003b). Because many of the toxicological attributes were scored in the mid-range at five due to lack of information presented in the papers (in particular, the attributes Contaminant Form, Test Concentration and Test Condition), relaxing the cut-off criteria helped ensure relevant papers are not inadvertently excluded.

After scoring the results, the results for each phase within a paper were reviewed for duplication within each major effect group. As called for in U.S. EPA (2007d), if more than one result was reported within a major effect group, the result with the most conservative result (i.e., the lowest NOAEL or LOAEL) was retained for TRV development. In cases where there were biochemical, behavior or pathology changes in the offspring, then two reproduction endpoints were coded, one reporting these effects in the parents, and the second in the offspring.

Mammalian Toxicity Reference Value

The literature search resulted in 298 citations and associated abstracts, which were reviewed for applicability in developing a mammalian TRV. Papers were obtained and reviewed for applicability in developing a mammalian TRV, and additional papers were identified and obtained from citations within reviewed papers. Ultimately, 123 papers were obtained and reviewed for applicability in developing a mammalian TRV. From these, 50 papers were identified as being relevant to the development of a mammalian TRV. These papers are listed in Table A-7. From these papers, 281 individual results were extracted and coded. After removing duplicate endpoints, a total of 201 discrete toxicological results remained, which are shown in Table 1.

The number of results coded in each major effect group are as follows:

Behavior:	23
Biochemistry:	28
Growth:	47
Mortality:	25
Physiology:	1
Pathology:	36
Reproduction:	33
Rejected:	8

The Agency for Toxic Substances and Disease Registry (ATSDR) recently revised their toxicological profile for uranium (ATSDR, 2011). Many of the results in Table 1 were also included in their profile. This is noted in the NOAEL/LOAEL comments column. Results that differ from what was presented in ATSDR (2011) are also noted. These differences occur in results in which the NOAEL and/or LOAEL had to be calculated from estimated body weights and intake rates. Differences were particularly apparent in the calculated values from Maynard and Hodge (1949). This paper was one of the earliest and most comprehensive papers published on the effects of various forms of uranium on the growth and mortality in rats, rabbits and dogs. Unfortunately, it was published before current standards of data presentation in journal papers. ATSDR (2011) does not report the values used in their calculations.

Figure 1 graphically presents the results from Table 1 for the biochemistry, pathology and behavior endpoints, and Figure 2 shows the mortality, growth and reproduction endpoints. These graphs were prepared as described in U.S. EPA (2007e), "*Guidance for Developing Ecological Soil Screening Levels (Eco-SSLs), Attachment 4-5, Standard Operating Procedure (SOP) #6: Derivation of Wildlife Toxicity Reference Value (TRV)"*. Closed symbols represent NOAELs and open symbols represent LOAELS. Paired NOAEL/LOAEL for the same endpoint are shown with a connecting line (these are referred to as bounded NOAEL/LOAELs). The result number on the x-axis of each figure corresponds to the result number in Table 1 for the given effect group.

When ingested, uranium found in the soluble forms uranium nitrate (also known as uranyl nitrate hexahydrate) and uranium acetate (also known as uranyl acetate dihydrate) is deposited throughout the body with the highest levels found in the bone, liver and kidney. The main target for toxicological effects is the kidney. Acute exposures to high levels of uranium can cause kidney damage. As shown in Table 1 and Figure 1, chronic exposure to low levels of soluble uranium can cause changes in blood and urine chemistry (under the effect group Biochemistry), as well as histological changes in the kidney and liver (under the effect group Pathology). These effects can occur at dosing levels less than 0.1 milligrams per kilogram per day (mg/kg/d), but generally occur at dosing levels over 1 mg/kg/d.

Behavioral effects include reduced spatial memory and travel distance, and occur at dosing levels greater than 1 mg/kg/d (under the effect group Behavior in Figure 1 and Table 1). Reduction in body weight gain of immature and juvenile animals can also occur at dosing levels greater than 1 mg/kg/d (under the effect group Growth in Table 1 and Figure 2).

At dosing levels greater than 1 mg/kg/d, soluble uranium can reduce the number of pups per litter, pup survival, the number of pregnant females in a population, and impact pup behavior (under the effect group Reproduction in Table 1 and Figure 2). Two LOAEL results, one showing histological changes in the liver of pups (result 18) and a second showing histological changes in the follicles of pups (result 19) were reported as dosing levels less than 0.1 mg/kg/d (Table 1 under the Reproduction effect group). Histological liver changes (result 18) would normally be of much lower significance and reported under the Pathology effect group. It is reported in the reproduction effect group as it was an effect on progeny exposed during gestation and lactation. The paper by Raymond-Wish et al. (2007) (result 19) was rejected by the Agency for Toxic Substances and Disease Registry (ATSDR) in their recent draft toxicological profile for uranium (ATSDR, 2011), as the effects appeared to be non-dose dependent and anomalously low. The authors themselves indicated the results appeared to be unrelated to uranium exposure.

Mortality from exposure to soluble uranium generally increases at dosing levels greater than 1 mg/kg/d (Figure 2). A single result from Dominigo et al. (1989b) reported a NOAEL of 0.28 mg/kg/d for mortality. Twenty female mice per dosing level were exposed by gavage to uranium acetate from day 13 of pregnancy through day 21 day of lactation (dosing levels were 0, 0.028, 0.28, 2.8 and 28 mg/kg/d of uranium). Two dams died at the 2.8 mg/kg/d dosing level and three dams died at the 28 mg/kg/d dosing level. The authors reported that although they did not investigate the cause of death, they attributed it to the administration of uranium.

With the exception of results from Maynard and Hodge (1949), all of the results in Table 1 and Figures 1 and 2 are for highly soluble uranium nitrate and uranium acetate. Maynard and Hodge (1949) investigated a variety of additional forms of uranium, which included the highly insoluble forms triuranium octoxide (U3O8) and uranium dioxide (UO2), as well as the slightly soluble forms uranium tetrafluoride (UF4) and uranium trioxide (UO3). The results for these forms, along with the species tested (RT=rat, DG=dog) are indicted in red in Figures 1 and 2. The highly insoluble forms of uranium had no impact on growth or mortality, where as the slightly soluble forms generally had some impact on growth and mortality (Figure 2).

A mammalian TRV was derived based on the protocol described in U.S. EPA (2007e), using a weight-of-evidence method. First, the geometric mean for the NOAEL results from the growth and reproduction effect groups was determined. The geometric mean from these effect groups is 12.28, and is shown on Figure 2. If only the results for uranium nitrate and uranium acetate are included (that is, the other forms of uranium are excluded, including the highly insoluble forms), the geometric mean is 6.7. Second, the geometric mean is examined with respect to bounded NOAEL and LOAEL results for the mortality, growth and reproduction effect groups. As can be seen in Figure 2, both 12.28 (the geometric mean for all the growth and reproduction results) and 6.7 (the geometric mean for only the uranium nitrate and uranium acetate results) is higher than numerous bounded NOAEL/LOAEL results. Further review of Figure 2 shows that a value of 1 mg/kg/d would be lower than all bound NOAEL/LOAEL results except for the mortality result from Domingo et al. (1989b). A value of 1 mg/kg/d would be between the NOEAL and LOAEL for this result. Thus, 1 mg/kg/d is lower than the lowest bounded LOAEL for the mortality, growth, and reproduction effect groups, and is consistent with U.S. EPA (2007e). Furthermore, a value of 1 mg/kg/d is lower than most of the NOAEL data in the biochemistry, pathology and behavior effect groups. Therefore, the weight-of-evidence of the toxicological data on uranium suggest a value of 1 mg of uranium/kg of body weight/day would be protective of mammalian wildlife in general, and deer mice in particular (as the vast majority of data come from mice and rats).

Avian Uranium Toxicity Reference Value

The literature search identified 26 citations and associated abstracts. Unfortunately, the vast majority of these were field studies reporting tissue concentration. A single oral study by Haseltine and Silo (1983), and a single acute study by Harvey et al. (1986), was identified. Although acute studies are typically rejected for the development of TRVs, the results from Harvey et al. (1986) was extracted as it could provide relevant information in interpreting the data from Haseltine and Silo (1983). Extracted data are shown in Table 2.

The acute study by Harvey et al. (1986) consisted of injecting uranium nitrate into 28-day-old leghorn chicks. The 7-day lethal dose (LD50) was determined to be 110 mg of uranium per kg of body weight, and the lowest lethal dose was 76 mg of uranium per kg of body weight, with the highest non-lethal dose being 62 mg of uranium per kg of body weight. The authors reported that this was 100 fold higher than that observed for rats or mice. Therefore, based on relatively limited data, it appears that birds are not as sensitive to the effects of uranium as compared to mammals. This was also the conclusion reached by Sheppard et al. (2005), who reviewed this study during the development of eco-toxicity thresholds for uranium.

The study by Haseltine and Silo (1983) was conducted on black ducks. This was a 6 week study in which adult ducks were fed a diet of 25, 100, 400 or 1600 parts per million (ppm) of uranium in mash. Endpoints measured were mortality, adult body weight, blood chemistry, liver, and kidney effects. No effects were observed at any dosing level. Sample et al. (1996) estimated a NOAEL of 160 mg/kg/d by assuming a body weight of 1.25 kg and a consumption rate of 125 gram (g) food/d. Sample et al. (1996) developed a toxicological benchmark by applying a safety factor of 0.1 because the study was considered sub-chronic as it lasted less than 10 weeks and did not consider a critical life stage such as reproduction. Sample et al. (1996) proposed a resulting Toxicity Reference Value (TRV) of 16 mg/kg/d.

Because of the limited toxicological data available, it is not possible to derive an avian TRV following a protocol based on U.S. EPA (2007e). Therefore, the TRV used in the Building 812 SLERA, that of 10 mg uranium/kg of body weight/day, will be used in the Building 812 BERA. This is 10 times higher than the mammalian TRV, and is consistent with the evidence that avian species are not sensitive species with respect to uranium exposure.

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Acronyms and Abbreviations

%	Percent
AD	Adult (adulthood)
adj	Adjusted
ADL	*ad libitum* (freely feeding or drinking)
Alt	Alternate
ATSDR	Agency for Toxic Substances and Disease Registry
B	Both sexes (male and female)
BERA	Baseline Ecological Risk Assessment
BRAWP	Baseline Risk Assessment Workplan
cmpd	Compound
conc	Concentration
d	Day
DLY	Daily
DOE	United States Department of Energy
DR	Drinking water
DU	Depleted uranium
DTSC	Department of Toxic Substances
DUAD	Depleted uranium (uranyl) acetate dihydrate; $UO_2(CH_3COO)_2$•2(H2O)
DUN	Depleted uranium (uranyl) nitrate hexahydrate; $UO_2(NO_3)_2$•6($H_2$0)
Eco-SSLs	Ecological Soil Screening Levels
EPA	United States Department of Energy
EU	Enriched uranium
EUN	Enriched uranium (uranyl) nitrate hexahydrate; $UO_2(NO_3)_2$•6($H_2$0)
exp	Exposure
F	Female
F0	Zero or initial generation
F1	First generation
FD	Food
g	Gram
gest	Gestation
grwth	Growth
GV	Gavage
IM	Immature
intk	Intake
JV	Juvenile
kg	Kilogram
L	Liter
lact	Lactation
LD25	Lethal Dose for 25% of the population
LD50	Lethal Dose for 50% of the population
LLNL	Lawrence Livermore National Laboratory
LOAEL	Lowest Observable Adverse Effect Level
M	Male
mate	Mating

meas	Measured
mg	Milligram
mo	Month
mtn	Maintain
MW	Molecular Weight
N	No
NA	Not Applicable
NaUO	Sodium uranium oxide; $Na_2U_2O_7$
NH4U2	Ammonium diurante; $(NH_4)_2U_2O_7$
No	Number
NOAEL	No Observable Adverse Effect Level
NR	Not Reported
PCOEC	Preliminary Contaminant of Ecological Concern
ppm	Parts per million
preg	Pregnancy
REM	Rapid eye movement
RWQCB	Regional Water Quality Control Board
SM	Sexually mature
SLERA	Screening-level ecological risk assessment
SOPs	Standard Operating Procedures
thru	Through
TRV	Toxicity Reference Value
trvl	Travel
U	Uranium
UA	Uranium (uranyl) acetate, assumed equivalent to uranium (uranyl) acetate dihydrate
UAD	Uranium (uranyl) acetate dihydrate; $UO_2(CH_3COO)_2$•2(H2O)
UCL4	Uranium tetrachloride; UCL_4
UF	Uranyl fluoride; UO_2F_2
UF4	Uranium tetrafluoride; UF_4
UN	Uranium (uranyl) nitrate, also known as uranium (uranyl) nitrate hexahydrate; $UO_2(NO_3)_2$•6(H_20)
U3O8	Triuranium octoxide; U_3O_8
UO2	Uranium dioxide; UO_2
UO3	Uranium trioxide; UO_3
UO4	Uranium peroxide; UO_4
untrt	Untreated
wk	Week
wt	Weight
Y	Yes
yr	Year

Figures

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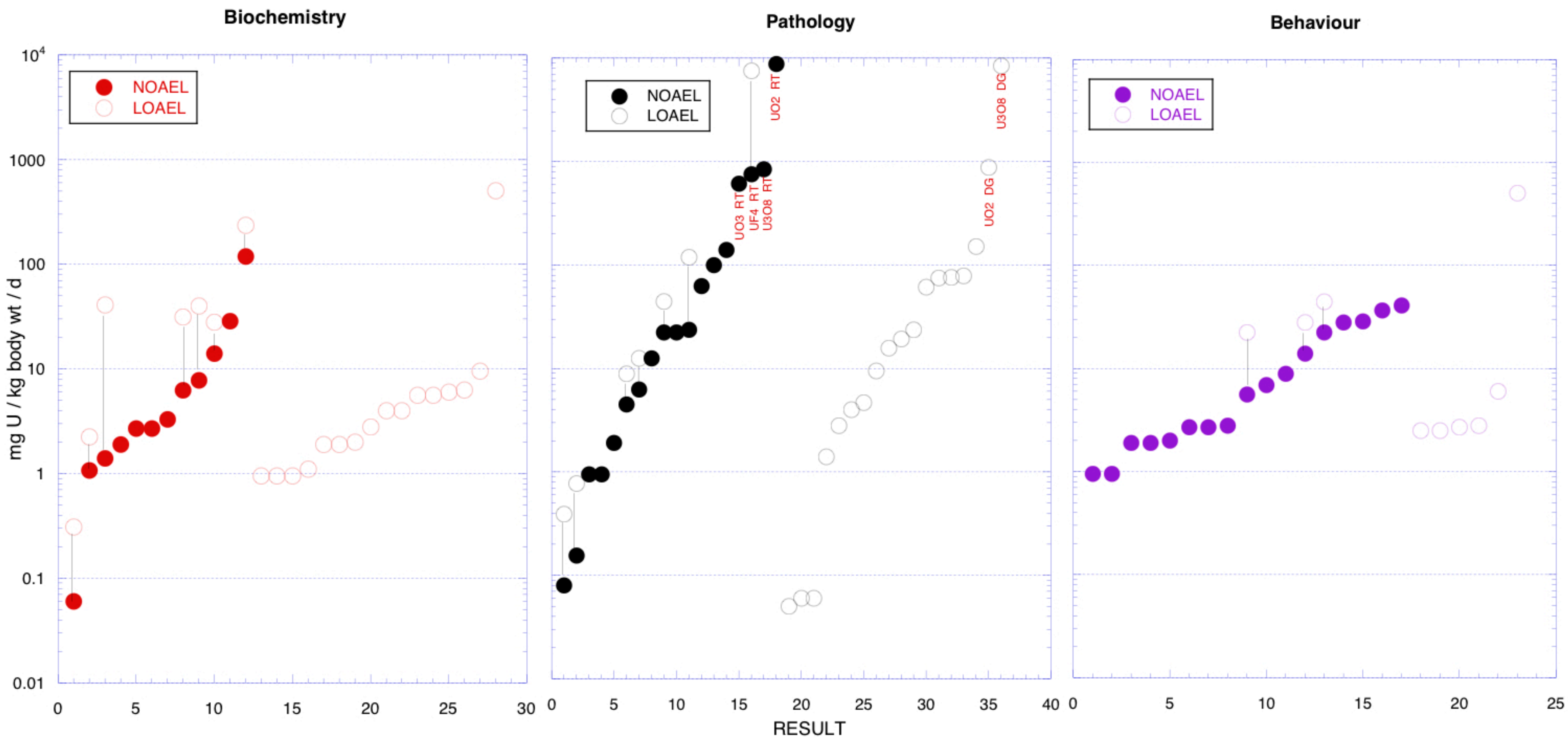

Figure 1. Mammalian uranium NOAEL and LOAEL data for biochemistry, pathology and behavior endpoints. Results of insoluble and slightly soluble forms of uranium from Maynard and Hodge (1949) identified by red captions. Slightly soluble forms: UO3=uranium trioxide, UF4=uranium tetrafluoride. Insoluble forms: U3O8=triuranium octoxide, UO2=uranium dioxide. Tests species: RT=rat, DG=dog.

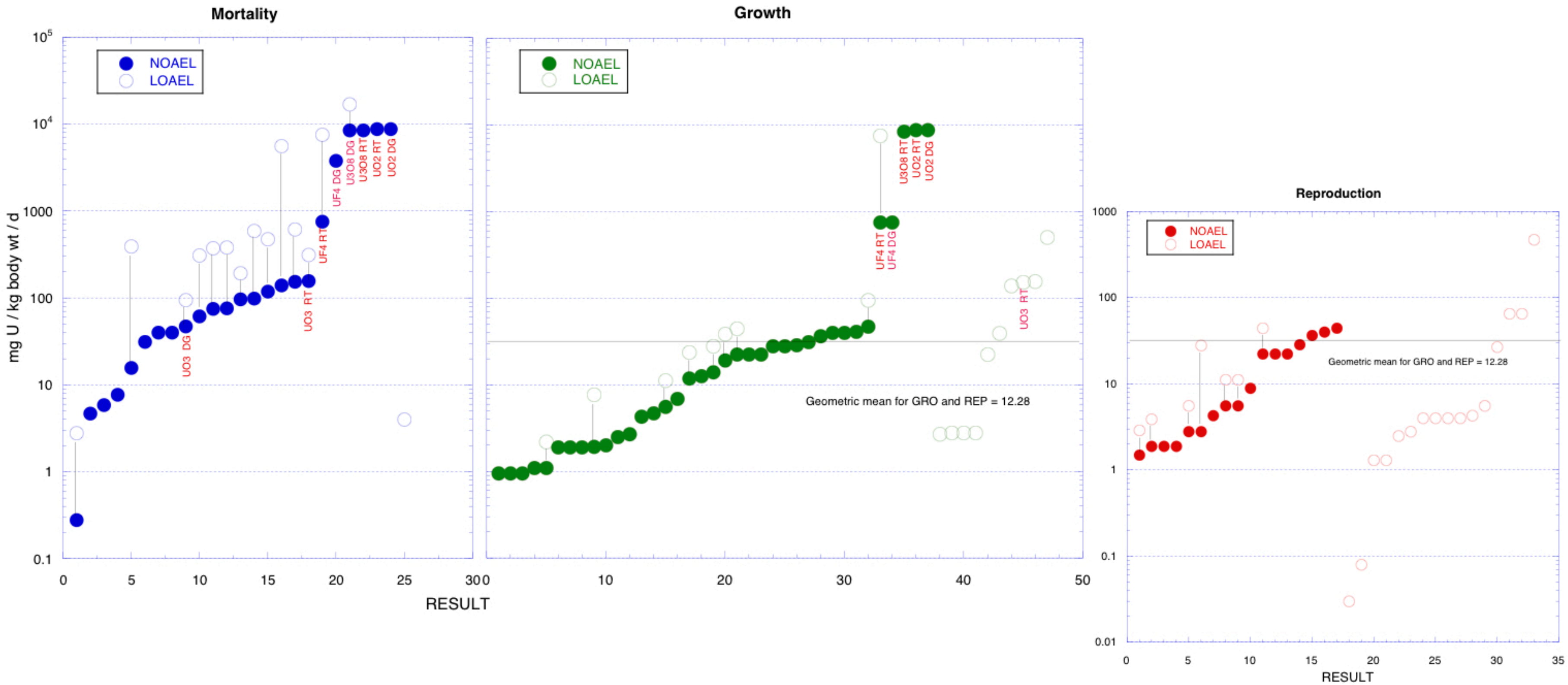

Figure 2. Mammalian uranium NOAEL and LOAEL data for mortality, growth and reproduction endpoints. Results of insoluble and slightly soluble forms of uranium from Maynard and Hodge (1949) identified by red captions. Slightly soluble forms: UO3=uranium trioxide, UF4=uranium tetrafluoride. Insoluble forms: U3O8=triuranium octoxide, UO2=uranium dioxide. Tests species: RT=rat, DG=dog.

Tables

List of Tables

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium.

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
BEHAVIOR EFFECT GROUP																																									
1	29	Lestaevel et al 2009	Depleted uranyl nitrate hexaahydrate	47.40%	rat	1	0, 2	mg DUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	BEH	FDB	CAIN/ WCON	Caloric/water intk	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	4	10	7	7	68
2	29	Lestaevel et al 2009	Enriched uranyl nitrate hexahydrate	47.40%	rat	2	0, 2	mg EUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	BEH	FDB	CAIN/ WCON	Caloric/water intk	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	4	10	7	7	68
3	19	Grignard et al 2008	Depleted uranyl nitrate hexahydrate	100%	rat	1	0, 40	mg/L DU	ADL	DR	9	mo		NR	NR	IM	M	BEH	FDB	CAIN	Caloric intk	40		Y	250	N	0.012	1.9			10	5	5	6	5	5	4	10	7	7	64
4	19	Grignard et al 2008	Enriched uranium nitrate	100%	rat	2	0, 40	mg/L EU	ADL	DR	9	mo		NR	NR	IM	M	BEH	FDB	CAIN	Caloric intk	40		Y	250	N	0.012	1.9			10	5	5	6	5	5	4	10	7	7	64
5	4	Bensoussan et al 2009	Uranyl nitrate hexahydratate	100%	rat	1	0, 2	mg U/kg/d	ADL	DR	9	mo	also meas at 1.5 and 9 mo	2	mo	IM	M	BEH	FDB	CAIN	Caloric intk	2		NA	NA	NA	NA	2			10	5	5	8	5	5	4	10	10	7	69
6	23	Houpert et al 2005	Depleted uranium nitrate	100%	rat	2	0, 40	mg DU/L	ADL	DR	1.5	mo		10	wk	IM	B	BEH	BEH	ACTP	Spatial memory	40		Y	370	Y	1 mg U/ d/rat	2.7		Reported in ATSDR 2011	10	5	5	7	5	5	4	10	7	4	62
7	50	Wade-Gueye et al 2012	Uranyl nitrate	100%	rat	2	0, 40	mg U/L	ADL	DR	9	mo	exp start at 3 mo	3	mo	IM	M	BEH	FDB	CAIN	Caloric intk	40		N	370	N	1 mg U/ d/rat	2.7			10	5	5	6	5	5	4	10	7	7	64
8	11	Bussy et al 2006	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 40	mg DUN/L	ADL	DR	9	mo	also meas at 1.5, 6 and 9 mo	NR	NR	IM	M	BEH	FDB	CAIN	Caloric intk	40		Y	200-250		1.4 to 4 mg U/d/rat end	2.8			10	5	5	7	5	5	4	10	7	7	65
9	3	Belles et al 2005	Uranyl acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo		NR	NR	IM	M	BEH	BEH	LOCO	Total Distance trvl	10	40	NA	NA	NA	NA	5.6	22.4	Reported in ATSDR 2011	10	5	5	10	8	5	4	10	7	7	71
10	14	Feugier et al 2008	Depleted uranium, NR	100%	mouse	1	0, 1.9, 3.9, 6.9	mg DU/kg/d	ADL	DR	49	d		4	wk	IM	F	BEH	FDB	CAIN	Caloric intk	6.9		NA	NA	NA	NA	6.9			10	5	5	10	5	8	4	10	7	7	71
11	40	Ortega et al 1989a	Uranyl acetate dihydrate	55.90%	rat	1	0, 2, 4, 8, 16	mg UAD/kg/d	ADL	DR	4	wk		NR	NR	IM	M	BEH	FDB	CAIN	Caloric intk	16						8.9			10	5	5	10	5	5	4	10	10	2	66
12	9	Briner and Murray 2005	Depleted uranium acetate dihydrate	55.90%	rat	1	0, 25, 50	mg DUAD/kg/d	ADL	DR	6	mo	also meas at 2 wk	8	mo	IM	M	BEH	BEH	ACTP	Maze tests	25	50	NA	NA	NA	NA	14.0	28.0	Reported in ATSDR 2011; same result at 2 wk	10	5	5	10	10	5	4	10	5	4	68
13	33	Linares et al 2008	Uranium acetate dihydrate	55.90%	rat	2	0, 40, 80	mg UAD/kg/d	ADL	DR	4	wk		NR	NR	SM	F	BEH	BEH	LOCO	Total Distance trvl	40	80	NA	NA	NA	NA	22.4	44.7		10	5	5	10	10	5	4	3	7	7	66
14	12	Domingo et al 1989b	Uranyl acetate dihydrate	55.90%	mouse	1	0, 0.05, 0.5, 5, 50	mg UAD/kg/d	DLY	GV	30	d	d 13 of preg to d 21 of lact	NR	NR	AD	F	BEH	FDB	CAIN	Maternal caloric intk	50		NA	NA	NA	NA	28.0			10	5	5	10	5	8	4	10	7	4	68
15	16	Gilman et al 1998 b	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 0.05, 0.20, 0.88, 4.82, 28.70	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	BEH	FDB	CAIN/ WCON	Caloric/water intk	28.7		NA	NA	NA	NA	28.7		F 43 mg/kg/d	10	5	5	10	5	5	4	10	10	4	68
16	15	Gilman et al 1998a	Uranyl nitrate hexahydrate	100%	rat	2	0, 0.06, 0.31, 1.52, 7.54, 36.73	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	BEH	FDB	CAIN/ WCON	Caloric/water intk	36.73		NA	NA	NA	NA	36.7		F 53.6 mg/kg/d	10	5	5	10	5	5	4	10	10	4	68
17	17	Gilman et al 1998c	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 1.36, 40.98	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	BEH	FDB	CAIN/ WCON	Caloric/water intk	40.98		NA	NA	NA	NA	41.0			10	5	5	10	5	5	4	10	10	4	68
18	25	Houpert et al 2007b	Enriched uranium nitrate	100%	rat	1	0, 40	mg EU/L	ADL	DR	9	mo		2.5	mo	IM	M	BEH	BEH	ACTP	Spatial memory		40	Y	402	Y	1 mg U/ d/rat		2.5	Reported in ATSDR 2011	10	5	5	7	4	5	4	10	10	7	67
19	28	Lestaevel et al 2005a	Uranium nitrate	100%	rat	1	0, 40	mg U/L	ADL	DR	90	d		12	wk	IM	M	BEH	BHE	INST	REM sleep		40	Y	402	Y	1 mg U/ d/rat		2.5	Reported by ATSDR 2011 as 3.7 mg/kg/d	10	5	5	7	4	5	4	10	10	7	67
20	23	Houpert et al 2005	Enriched uranium nitrate	100%	rat	1	0, 40	mg EU/L	ADL	DR	1.5	mo		10	wk	IM	B	BEH	BEH	ACTP	Spatial memory		40	Y	370	Y	1 mg U/ d/rat		2.7	Reported in ATSDR 2011	10	5	5	7	4	5	4	10	7	4	61
21	13	Dominigo et al 1989c	Uranyl acetate dihydrate	55.90%	mouse	1	0, 5, 10, 25, 50	mg UAD/kg/d	DLY	GV	10	d	d 6 to 15 of gest	NR	NR	AD	F	BEH	FDB	CAIN	Caloric intk		5	NA	NA	NA	NA		2.8		10	5	5	10	4	8	4	10	10	4	70
22	10	Briner 2009	Depleted uranyl acetate dihydrate	100.00%	mouse	1	0, 6	mg DU/kg/d	ADL	DR	2	wk		30	d	IM	F	BEH	BEH	NMVM	Open field test line crossings		6	NA	NA	NA	NA		6	Reported in ATSDR 2011	10	5	5	10	4	5	4	10	7	7	67
23	41	Ozmen and Yurekli 1998	Uranyl acetate dihydrate	55.90%	mouse	1	0, 905	mg UAD/kg/d	ADL	FD	5	d		NR	NR	IM	M	BEH	FDB	CAIN	Caloric intk		905	NA	NA	NA	NA		506		10	5	5	10	4	10	4	10	10	4	72
BIOCHEMISTRY EFFECT GROUP																																									
1	15	Gilman et al 1998a	Uranyl nitrate hexahydrate	100%	rat	2	0, 0.06, 0.31, 1.52, 7.54, 36.73	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	BIO	CHM	Various	Hemotological and biochemical	0.06	0.31	NA	NA	NA	NA	0.06	0.31	F 0.42 and 2.01 mg/kg/d	10	5	5	10	8	5	1	10	10	4	68
2	35	Mahmoudzadeh et al 2007	Uranyl nitrate hexahydrate	44.70%	rabbit	1	0, 24, 500	mg UN/L	ADL	DR	90	d		NR	NR	IM	M	BIO	CHM	GLUC	Urinary glucose	24	50	Y	1200	N	0.12	1.073	2.24		10	5	5	6	10	5	1	10	7	2	61
3	17	Gilman et al 1998c	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 1.36, 40.98	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	BIO	CHM	GLUC	Blood Glucose	1.36	40.98	NA	NA	NA	NA	1.4	41.0		10	5	5	10	8	5	1	10	10	4	68
4	19	Grignard et al 2008	Depleted uranyl nitrate hexahydrate	100%	rat	1	0, 40	mg DU/L	ADL	DR	9	mo		NR	NR	IM	M	BIO	HRM	TSTR	Testorone production	40		Y	250	N	0.012	1.9		Reported in ATSDR 2011	10	5	5	6	5	5	1	10	10	7	64
5	50	Wade-Gueye et al 2012	Uranyl nitrate	100%	rat	1	0, 40	mg U/L	ADL	DR	9	mo	lact thru 9 mo	0	d	IM	M	BIO	CHM	CREA	Creatine	40		N	370	N	1 mg U/ d/rat	2.7			10	5	5	6	5	5	1	10	10	7	64
6	50	Wade-Gueye et al 2012	Uranyl nitrate	100%	rat	2	0, 40	mg U/L	ADL	DR	9	mo	exp start at 3 mo	3	mo	IM	M	BIO	CHM	CREA	Creatine	40		N	370	N	1 mg U/ d/rat	2.7			10	5	5	6	5	5	1	10	10	7	64
7	22	Houpert et al 2004	Depleted uranium, NR	100%	rat	1	0, 40	mg DU/L	ADL	DR	30	d		NR	NR	IM	M	BIO	HRM	DOPA	Dopamine levels	40		Y	300	Y	1 mg U/ d/rat	3.3			10	4	5	7	5	5	1	10	7	7	61

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
BIOCHEMISTRY EFFECT GROUP (continued)																																									
8	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	dog	25	cntl, 0.002, 0.01, 0.05	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	BIO	CHM	Renal	Urine sugar, urine protein	0.01	0.05					6.27	31.4	ATSDR 2011 reports.	10	5	5	10	8	10	1	10	3	2	64
9	15	Gilman et al 1998a	Uranyl nitrate hexahydrate	100%	rat	1	0, 0.07, 0.33, 1.65, 7.82, 40	mg U/kg/d	ADL	DR	28	d		NR	NR	JV	F	BIO	CHM	URIC	Uric acid in serum	7.82	40	NA	NA	NA	NA	7.8	40	Reported in ATSDR 2011, M NOAEL 35 mg/kg/d	10	5	5	10	8	5	1	10	7	4	65
10	9	Briner and Murray 2005	Depleted uranium acetate dihydrate	55.90%	rat	1	0, 25, 50	mg DUAD/kg/d	ADL	DR	6	mo	also meas at 2 wk	8	mo	IM	B	BIO	CHM	LPSA	Lipid oxidation	25	50	NA	NA	NA	NA	14.0	28.0	Same result at 2 wk	10	5	5	10	10	5	1	10	5	4	65
11	16	Gilman et al 1998 b	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 0.05, 0.20, 0.88, 4.82, 28.70	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	BIO	CHM		Hemotological and biochemical	28.7		NA	NA	NA	NA	28.7		Reported in ATSDR 2011; F 43 mg/kg/d	10	5	5	10	5	5	1	10	10	4	65
12	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rat	11	0, 0.01, 0.05, 0.1, 0.5, 1, 2	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	F	BIO	CHM		Anemia	0.50%	1.00%	Y	300	Y	15	119	237		10	5	5	7	10	10	1	10	3	2	63
13	29	Lestaevel et al 2009	Depleted uranyl nitrate hexaahydrate	47.40%	rat	1	0, 2	mg DUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	BIO	ENZ		Catalase activity		2	NA	NA	NA	NA		0.95		10	5	5	10	4	5	1	10	7	7	64
14	29	Lestaevel et al 2009	Enriched uranyl nitrate hexahydrate	47.40%	rat	2	0, 2	mg EUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	BIO	ENZ		Catalase activity		2	NA	NA	NA	NA		0.95		10	5	5	10	4	5	1	10	7	7	64
15	43	Racine et al 2010	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 2	mg UN/kg/d	ADL	DR	9	mo		12	wk	IM	M	BIO	CHM	CHOL	Cholesterol		2	NA	NA	NA	NA		0.95	Reported by ATSDR 2011 as 1 mg/kg/d	10	5	5	10	4	5	1	10	10	7	67
16	40	Ortega et al 1989a	Uranyl acetate dihydrate	55.90%	rat	1	0, 2, 4, 8, 16	mg UAD/kg/d	ADL	DR	4	wk		NR	NR	IM	M	BIO	CHM	PRTL	Protein, total		2						1.1	Reported in ATSDR 2011	10	5	5	10	4	5	1	10	10	2	62
17	47	Souidi et al 2005	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 40	mg DUN/L	ADL	DR	9	mo		NR	NR	IM	M	BIO	CHM	CHOL	Cholesterol		40	Y	250	Y	1 mg U/ d/rat		1.9		10	5	5	7	4	5	1	10	10	7	64
18	19	Grignard et al 2008	Enriched uranium nitrate	100%	rat	2	0, 40	mg EU/L	ADL	DR	9	mo		NR	NR	IM	M	BIO	HRM	TSTR	Testorone production		40	Y	250	N	0.012		1.9	Reported in ATSDR 2011	10	5	5	6	4	5	1	10	10	7	63
19	4	Bensoussan et al 2009	Uranyl nitrate hexahydrate	100%	rat	1	0, 2	mg U/kg/d	ADL	DR	9	mo	also meas at 1.5 and 9 mo	2	mo	IM	M	BIO	ENZ	ACHE	Acetyl-cholinesterase		2	NA	NA	NA	NA		2	Reported by ATSDR 2011	10	5	5	8	4	5	1	10	7	7	62
20	11	Bussy et al 2006	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 40	mg DUN/L	ADL	DR	9	mo	also meas at 1.5, 6 and 9 mo	NR	NR	IM	M	BIO	ENZ	ACHE	Acetyl-cholinestrase		40	Y	200-250		1.4 to 4 mg U/d/rat end		2.8		10	5	5	7	4	5	1	10	7	7	61
21	5	Berradi et al 2008	Depleted uranium, NR	100%	rat	1	0, 40	mg DU/L	ADL	DR	9	mo		3	mo	IM	M	BIO	CHM	RBCE	Red blood cell count		40	Y	250		1 mg U/ d/rat		4	Reported by ATSDR 2011 as 1 mg/kg/d	10	4	5	7	4	5	1	10	10	7	63
22	49	Tissandie et al 2007	Depleted uranyl nitrate hexahydrate	100%	rat	1	0, 40	mg DU/L	ADL	DR	9	mo		12	wk	IM	M	BIO	CHM	VTD3	Vitamin D3		40	Y	250	Y	1 mg U/ d/rat		4.0	Reported by ATSDR 2011 as 1 mg/kg/d	10	5	5	7	4	5	1	10	10	7	64
23	31	Linares et al 2006	Uranyl acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo	Conc adj to mtn dose thru grwth	NR	NR	SM	M	BIO	ENZ		Catalase		10	NA	NA	NA	NA		5.6		10	5	5	10	4	5	1	10	7	7	64
24	32	Linares et al 2007	Uranyl acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo	Conc adj to mtn dose thru grwth	NR	NR	SM	M	BIO	ENZ		Catalase		10	NA	NA	NA	NA		5.6		10	5	5	10	4	5	1	10	10	7	67
25	10	Briner 2009	Depleted uranyl acetate dihydrate	100.00%	mouse	1	0, 6	mg DU/kg/d	ADL	DR	2	wk		30	d	IM	B	BIO	HRM	DOPA	Dopamine		6	NA	NA	NA	NA		6		10	5	5	10	4	5	1	10	7	7	64
26	48	Taulan et al 2004	Uranyl nitrate	47.40%	mouse	1	0, 80, 160	mg UN/L	ADL	DR	4	mo		NR	NR	IM	M	BIO	CHM	CREA	Creatinine		80	Y	25-30	N	0.005		6.3		10	5	5	6	4	5	1	10	10	2	58
27	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	dog	26	0, 0.02, 0.1, 0.2	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	BIO	CHM		Urine sugar, urine protein		0.02						9.5		10	5	5	10	4	10	1	10	3	2	60
28	41	Ozmen and Yurekli 1998	Uranyl acetate dihydrate	55.90%	mouse	1	0, 905	mg UAD/kg/d	ADL	FD	5	d		NR	NR	IM	M	BIO	CHM	BUNT, CREA	Blood urea nitrogen, creatinine		905	NA	NA	NA	NA		506	Reported by ATSDR 2011 as 508 mg/kg/d	10	5	5	10	4	10	1	10	10	4	69
GROWTH EFFECT GROUP																																									
1	29	Lestaevel et al 2009	Depleted uranyl nitrate hexaahydrate	47.40%	rat	1	0, 2	mg DUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	8	10	10	7	75
2	29	Lestaevel et al 2009	Enriched uranyl nitrate hexahydrate	47.40%	rat	2	0, 2	mg EUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	8	10	10	7	75
3	43	Racine et al 2010	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 2	mg DUN/kg/d	ADL	DR	9	mo		12	wk	IM	M	GRO	GRO	BDWT	Body wt gain	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	8	10	7	7	72
4	45	Rouas et al 2011	Depleted Uranyl nitrate	47.40%	rat	1	0, 40	mg UN/L	ADL	DR	9	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	40		Y	250	Y	1 mg UN/ d/rat	1.1			10	5	5	7	5	5	8	10	5	2	62
5	40	Ortega et al 1989a	Uranyl acetate dihydrate	55.90%	rat	1	0, 2, 4, 8, 16	mg UAD/kg/d	ADL	DR	4	wk		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	2	4					1.1	2.2		10	5	5	10	10	5	8	10	10	2	75
6	47	Souidi et al 2005	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 40	mg DUN/L	ADL	DR	9	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	40		Y	250	Y	1 mg U/ d/rat	1.9			10	5	5	7	5	5	8	10	10	7	72

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
GROWTH EFFECT GROUP (continued)																																									
7	19	Grignard et al 2008	Depleted uranyl nitrate hexahydrate	100%	rat	1	0, 40	mg DU/L	ADL	DR	9	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	40		Y	250	N	0.012	1.9			10	5	5	6	5	5	8	10	7	7	68
8	19	Grignard et al 2008	Enriched uranium nitrate	100%	rat	2	0, 40	mg EU/L	ADL	DR	9	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	40		Y	250	N	0.012	1.9			10	5	5	6	5	5	8	10	7	7	68
9	37	Maynard and Hodge 1949	uranyl fluoride	77.30%	dog	24	cntl, 0.0002, 0.001, 0.0025, 0.01	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	GRO	GRO	BDWT	Body weight	0.0025	0.01					1.93	7.73		10	5	5	10	8	10	8	10	3	2	71
10	4	Bensoussan et al 2009	Uranyl nitrate hexahydratate	100%	rat	1	0, 2	mg U/kg/d	ADL	DR	9	mo	also meas at 1.5 and 9 mo	2	mo	IM	M	GRO	GRO	BDWT	Body wt gain	2		NA	NA	NA	NA	2.0		Reported by ATSDR 2011	10	5	5	8	5	5	8	10	10	7	73
11	28	Lestaevel et al 2005a	Uranium nitrate	100%	rat	1	0, 40	mg U/L	ADL	DR	90	d		12	wk	IM	M	GRO	GRO	BDWT	Body wt gain	40		Y	402	Y	1 mg U/ d/rat	2.5			10	5	5	7	5	5	8	10	7	7	69
12	50	Wade-Gueye et al 2012	Uranyl nitrate	100%	rat	2	0, 40	mg U/L	ADL	DR	9	mo	exp start at 3 mo	3	mo	IM	M	GRO	MPH		Cortical bone parameters femur	40		N	370	N	1 mg U/ d/rat	2.7			10	5	5	6	5	5	8	10	10	7	71
13	24	Houpert et al 2007a	Enriched uranium nitrate	100%	rat	1	0, 40	mg EU/L	ADL	DR	3	mo	M/F exp 3 mo, F exp thru gest/lact	8	wk	IM	B	GRO	GRO	BDWT	Body wt gain in gest	40		N	230	Y	1 mg U/ d/rat	4.3			10	5	5	6	5	5	8	10	7	7	68
14	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rabbit	29	0, 0.02, 0.1, 0.5	% in diet	ADL	FD	30	d		NR	NR	IM	NR	GRO	GRO	BDWT	Body wt gain	0.02%	0.10%	N				4.7		10 mg/kg/d as cmpd reported by author	10	5	5	7	5	10	8	10	3	2	65
15	1	Albina et al 2005	Uranyl acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo	mated with untrt F	NR	NR	AD	M	GRO	GRO	BDWT	Body wt gain in gest	10	20	NA	NA	NA	NA	5.6	11.2		10	5	5	10	8	5	8	10	10	7	78
16	14	Feugier et al 2008	Depleted uranium, NR	100%	mouse	1	0, 1.9, 3.9, 6.9	mg DU/kg/d	ADL	DR	49	d		4	wk	IM	F	GRO	GRO	BDWT	Body wt gain	6.9		NA	NA	NA	NA	6.9			10	5	5	10	5	5	8	10	7	7	72
17	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rat	11	0, 0.01, 0.05, 0.1, 0.5, 1, 2	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	0.05%	0.10%	Y	300	Y	15	11.9	23.7		10	5	5	7	10	10	8	10	3	2	70
18	48	Taulan et al 2004	Uranyl nitrate	47.40%	mouse	1	0, 80, 160	mg UN/L	ADL	DR	4	mo		NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain	160		Y	25-30	N	0.005	12.6			10	5	5	6	5	5	8	10	5	2	61
19	9	Briner and Murray 2005	Depleted uranium acetate dihydrate	55.90%	rat	1	0, 25, 50	mg DUAD/kg/d	ADL	DR	6	mo	also meas at 2 wk	8	mo	IM	B	GRO	GRO	BDWT	Body wt gain	25	50	NA	NA	NA	NA	14.0	28.0	Reported in ATSDR 201; same results at 2 wk	10	5	5	10	10	5	8	10	5	4	72
20	37	Maynard and Hodge 1949	uranyl fluoride	77.30%	rat	10	cntl, 0.01, 0.05, 0.1, 0.15, 0.25, 0.50,	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	B	GRO	GRO	BDWT	Body weight	0.05%	0.10%	Y	300	Y	15	19.3	38.7	ATSDR 2011 reports 135.2 and 270	10	5	5	7	10	10	8	10	3	2	70
21	46	Sanchez et al 2006a	Uranyl acetate dihydrate	55.90%	rat	1	0, 40, 80	mg UAD/kg/d	ADL	DR	6	wk	4 wk prior to mate, gest, lact	NR	NR	AD	B	GRO	GRO	BDWT	Body wt gain in gest	40	80	NA	NA	NA	NA	22.4	44.7		10	5	5	10	10	5	8	10	10	7	80
22	1	Albina et al 2005	Uranyl acetate dihydrate	55.90%	rat	2	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo	mated with untrt F	NR	NR	AD	M	GRO	GRO	BDWT	Pup wt at 21 d	40		NA	NA	NA	NA	22.4			10	5	5	10	5	5	8	10	10	7	75
23	30	Linares et al 2005	Uranium acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo		NR	NR	SM	M	GRO	GRO	BDWT	Body wt gain in gest	40		NA	NA	NA	NA	22.4			10	5	5	10	5	5	8	10	10	7	75
24	12	Domingo et al 1989b	Uranyl acetate dihydrate	55.90%	mouse	1	0, 0.05, 0.5, 5, 50	mg UAD/kg/d	DLY	GV	30	d	d 13 of preg to d 21 of lact	NR	NR	AD	F	GRO	GRO	BDWT	Body wt gain in gest	50		NA	NA	NA	NA	28.0			10	5	5	10	5	8	8	10	7	4	72
25	12	Domingo et al 1989b	Uranyl acetate dihydrate	55.90%	mouse	2	0, 0.05, 0.5, 5, 50	mg UAD/kg/d	DLY	GV	30	d	d 13 of preg to d 21 of lact	NR	NR	AD	F	GRO	GRO	BDWT	Pup wt at 21 d	50		NA	NA	NA	NA	28.0			10	5	5	10	5	8	10	10	10	4	77
26	16	Gilman et al 1998 b	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 0.05, 0.20, 0.88, 4.82, 28.70	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	GRO	GRO	BDWT	Body wt gain	28.7		NA	NA	NA	NA	28.7		Reported in ATSDR 2011; F 43 mg/kg/d	10	5	5	10	5	5	8	10	10	4	72
27	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	dog	25	cntl, 0.002, 0.01, 0.05	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	GRO	GRO	BDWT	Body weight	0.05						31.35			10	5	5	10	5	10	8	10	3	2	68
28	15	Gilman et al 1998a	Uranyl nitrate hexahydrate	100%	rat	2	0, 0.06, 0.31, 1.52, 7.54, 36.73	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	GRO	GRO	BDWT	Body wt gain	36.73		NA	NA	NA	NA	36.7		Reported in ATSDR 2011; F 53.6 mg/kg/d	10	5	5	10	5	5	8	10	10	4	72
29	21	Hao et al 2012	Depleted uranium uranyl nitrate	100%	rat	2	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	3 wk to 4 mo, M/ F	3	wk	IM	F0 F	GRO	GRO	BDWT	Pup wt at 21 d	40		NA	NA	NA	NA	40.0			10	5	5	10	5	10	8	10	10	7	80
30	21	Hao et al 2012	Depleted uranium uranyl nitrate	100%	rat	5	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	gest to death, M/ F	0	d	IM	F1 F	GRO	GRO	BDWT	Pup wt at 21 d	40		NA	NA	NA	NA	40.0		F0 NOAEL 40 mg/kg/d	10	5	5	10	5	10	8	10	10	7	80
31	17	Gilman et al 1998c	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 1.36, 40.98	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	GRO	GRO	BDWT	Body wt gain	40.98		NA	NA	NA	NA	41.0		Reported in ATSDR 2011	10	5	5	10	5	5	8	10	10	4	72
32	37	Maynard and Hodge	Uranyl nitrate hexahydrate	47.40%	dog	26	0, 0.02, 0.1, 0.2	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	GRO	GRO	BDWT	Body wt gain	0.1	0.2					47.4	94.8		10	5	5	10	10	10	8	10	3	2	73
33	37	Maynard and Hodge 1949	uranium tetrafluoride	75.80%	rat	12	cntl, 0.5, 2, 20	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	B	GRO	GRO	BDWT	Body weight	2%	20%	Y	300	Y	15	758	7580	ATSDR 2011 reports NOAEL of 10611	10	5	5	7	8	10	8	10	3	2	68
34	37	Maynard and Hodge	uranium tetrafluoride	75.80%	dog	28	cntl, 0.2, 1, 5	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	GRO	GRO	BDWT	Body weight	1	5					758			10	5	5	10	5	10	8	10	3	2	68
35	37	Maynard and Hodge 1949	triuranium octoxide	84.80%	rat	8	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	GRO	GRO	BDWT	Body weight	20%		Y	300	Y	15	8480		10,000 mg/kg/d as cmpd (8480 as U) by author	10	5	5	7	5	10	8	10	3	2	65

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
GROWTH EFFECT GROUP (continued)																																									
36	37	Maynard and Hodge 1949	uranium dioxide	88.20%	rat	13	cntl, 0.5, 2, 20	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	B	GRO	GRO	BDWT	Body weight	20%		Y	300	Y	15	8820		ATSDR 2011 reports 12341	10	5	5	7	5	10	8	10	3	2	65
37	37	Maynard and Hodge	uranium dioxide	88.20%	dog	27	cntl, 1, 5, 10	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	GRO	GRO	BDWT	Body weight	10						8820			10	5	5	10	5	10	8	10	3	2	68
38	50	Wade-Gueye et al 2012	Uranyl nitrate	100%	rat	1	0, 40	mg U/L	ADL	DR	9	mo	lact thru 9 mo	0	d	IM	M	GRO	MPH		Cortical bone parameters femur		40	N	370	N	1 mg U/ d/rat		2.7		10	5	5	6	4	5	8	10	10	7	70
39	13	Dominigo et al 1989c	Uranyl acetate dihydrate	55.90%	mouse	1	0, 5, 10, 25, 50	mg UAD/kg/d	DLY	GV	10	d	d 6 to 15 of gest	NR	NR	AD	F	GRO	GRO	BDWT	Body wt gain in gest		5	NA	NA	NA	NA		2.8	Reported in ATSDR 2011	10	5	5	10	4	8	8	10	10	4	74
40	42	Paternain et al 1989	Uranyl acetate dihydrate	55.90%	mouse	2	0, 5, 10, 25	mg UAD/kg/d	DLY	GV	60	d	M 60 d prior mate, F 14 d	NR	NR	AD	B	GRO	GRO	BDWT	Pup wt at 21 d		5	NA	NA	NA	NA		2.8	Reported in ATSDR 2011	10	5	5	10	4	8	8	10	10	4	74
41	11	Bussy et al 2006	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 40	mg DUN/L	ADL	DR	9	mo	also meas at 1.5, 6 and 9 mo	NR	NR	IM	M	GRO	GRO	BDWT	Body wt gain		40	Y	200-250		1.4 to 4 mg U/d/rat end		2.8		10	5	5	7	4	5	8	10	10	7	71
42	46	Sanchez et al 2006a	Uranyl acetate dihydrate	55.90%	rat	2	0, 40, 80	mg UAD/kg/d	ADL	DR	12	wk	4 wk prior to mate, gest, lact	NR	NR	AD	B	GRO	GRO	BDWT	Pup wt at 21 d		40	NA	NA	NA	NA		22.4	Reported in ATSDR 2011	10	5	5	10	4	5	8	10	10	7	74
43	37	Maynard and Hodge 1949	uranium peroxide	78.80%	rat	3	cntl, 20, 2, 1, 0.5, 0.25, 0.1	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	GRO	GRO	BDWT	Body weight		0.10%	Y	300	Y	15		39.4	50 mg/kg/das cmpd (39.4 as U) by author	10	5	5	7	4	10	8	10	3	2	64
44	37	Maynard and Hodge 1949	Uranium acetate	55.90%	rat	6	0, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	GRO	GRO	BDWT	Body wt gain		0.50%	Y	300	Y	15		140	250 mg/kg/d as cmpd (139.75 as U) by author	10	5	5	7	4	10	8	10	3	2	64
45	37	Maynard and Hodge 1949	uranium trioxide	61.60%	rat	5	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	GRO	GRO	BDWT	Body weight		0.50%	Y	300	Y	15		154	250 mg/kg/d as cmpd (154 as U) by author	10	5	5	7	4	10	8	10	3	2	64
46	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	rat	2	cntl, 0.2, 0.5, 1, 1.5, 2, 3, 20	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	GRO	GRO	BDWT	Body weight		0.50%	Y	300	Y	15		157	250 mg/kg/d as cmpd (156.75 as U) by author	10	5	5	7	4	10	8	10	3	2	64
47	41	Ozmen and Yurekli 1998	Uranyl acetate dihydrate	55.90%	mouse	1	0, 905	mg UAD/kg/d	ADL	FD	5	d		NR	NR	IM	M	GRO	FDB	BDWT	Body wt gain		905	NA	NA	NA	NA		506	Reported by ATSDR 2011 as 508 mg/kg/d as a NOAEL	10	5	5	10	4	10	8	10	10	4	76
MORTALITY EFFECT GROUP																																									
1	12	Domingo et al 1989b	Uranyl acetate dihydrate	55.90%	mouse	1	0, 0.05, 0.5, 5, 50	mg UAD/kg/d	DLY	GV	30	d	d 13 of preg to d 21 of lact	NR	NR	AD	F	MOR	MOR	GMOR	Mort during gest	0.5	5	NA	NA	NA	NA	0.28	2.8	Reported in ATSDR 2011	10	5	5	10	8	8	9	10	3	4	72
2	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rabbit	29	0, 0.02, 0.1, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.02%	0.10%	N				4.7		10 mg/kg/d as cmpd reported by author	10	5	5	7	5	10	9	10	3	2	66
3	6	Briner and Byrd 2000, Briner and Abboud 2002	Uranium acetate	55.90%	mouse	1	0, 19, 37, 75	mg UAD/L	ADL	DR	55	d	2 wks prior to mate, gest, lact	NR	NR	AD	F	MOR	MOR	MORT	Dam Mortality	75		N	28	N	0.004	5.9			10	5	5	5	5	5	9	10	5	4	63
4	37	Maynard and Hodge 1949	uranyl fluoride	77.30%	dog	24	cntl, 0.0002, 0.001, 0.0025, 0.01	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.01						7.73			10	5	5	10	5	10	9	10	3	2	69
5	37	Maynard and Hodge 1949	uranium peroxide	78.80%	dog	16	cntl, 0.02, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.02	0.5					15.76	394	ATSDR 2011 reports LOAEL	10	5	5	10	7	8	9	10	3	2	69
6	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	dog	25	cntl, 0.002, 0.01, 0.05	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.05						31.35			10	5	5	10	5	10	9	10	3	2	69
7	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	1	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	3 wk to 4 mo,	3	wk	IM	F0 F	MOR	MOR	SURV	Survival rate at 4 d	40		NA	NA	NA	NA	40.0			10	5	5	10	5	10	9	10	10	7	81
8	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	2	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	3 wk to 4 mo,	3	wk	IM	F0 F	MOR	MOR	SURV	Survival rate at 21	40		NA	NA	NA	NA	40.0			10	5	5	10	5	10	9	10	10	7	81
9	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	dog	26	0, 0.02, 0.1, 0.2	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.1	0.2					47.4	94.8		10	5	5	10	10	10	9	10	3	2	74
10	37	Maynard and Hodge 1949	uranium trioxide	61.60%	dog	18	cntl, 0.1, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.1	0.5					61.6	308		10	5	5	10	8	8	9	10	3	2	70
11	37	Maynard and Hodge 1949	sodium urnaium oxide	75.10%	dog	19	cntl, 0.1, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	MOR	HIS	MORT	Mortality	0.1	0.5					75.1	375.5	ATSDR 2011 reports 375.5 as LOAEL	10	5	5	10	8	8	9	10	3	2	70
12	37	Maynard and Hodge 1949	ammonium diurante	76.30%	dog	20	cntl, 0.1, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	0.1	0.5					76.3	381.5	ATSDR 2011 reports 191 as LOAEL	10	5	5	10	8	8	9	10	3	2	70
13	37	Maynard and Hodge 1949	uranyl fluoride	77.30%	rat	10	cntl, 0.01, 0.05, 0.1, 0.15, 0.25, 0.50	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	M	MOR	MOR	MORT	Mortality	0.25%	0.50%	Y	300	Y	15	96.6	193	ATSDR 2011 reports 135.2	10	5	5	7	10	10	9	10	3	2	71
14	37	Maynard and Hodge 1949	uranium peroxide	78.80%	rat	3	cntl, 20, 2, 1, 0.5, 0.25, 0.50	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	M	MOR	MOR	MORT	Mortality	0.25%	1.50%	Y	300	Y	15	98.5	591	LOAEL is an LD50	10	5	5	7	8	10	9	10	3	2	69

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
15	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rat	4	0, 0.1, 0.5, 1, 2, 3, 5, 10	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	MOR	MOR	MORT	Mortality	0.50%	2%	Y	300	Y	15	119	474	LOAEL is an LD25 for weanlings	10	5	5	7	8	10	9	10	3	2	69
MORTALITY EFFECT GROUP (continued)																																									
16	37	Maynard and Hodge 1949	Uranium acetate	55.90%	rat	6	0, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	M	MOR	MOR	MORT	Mortality	0.50%	20%	Y	300	Y	15	140	5590	LOAEL is 100% mortality	10	5	5	7	5	10	9	10	3	2	66
17	37	Maynard and Hodge 1949	uranium trioxide	61.60%	rat	5	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	M	MOR	MOR	MORT	Mortality	0.50%	2%	Y	300	Y	15	154	616	LOAEL is 100% mortality	10	5	5	7	5	10	9	10	3	2	66
18	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	rat	2	cntl, 0.2, 0.5, 1, 1.5, 2, 3, 20	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	M	MOR	MOR	MORT	Mortality	0.50%	1%	Y	300	Y	15	156.8	313.5	LOAEL is an LD50	10	5	5	7	10	10	9	10	3	2	71
19	37	Maynard and Hodge 1949	uranium tetrafluoride	75.80%	rat	9	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	MOR	MOR	MORT	Mortality	2%	20%	Y	300	Y	15	758	7580		10	5	5	7	8	10	9	10	3	2	69
20	37	Maynard and Hodge 1949	uranium tetrafluoride	75.80%	dog	28	cntl, 0.2, 1, 5	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	5						3790			10	5	5	10	5	10	9	10	3	2	69
21	37	Maynard and Hodge 1949	triuranium octoxide	84.80%	dog	22	cntl, 10, 20	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	10	20					8480	16960	ATSDR 2011 reports 5653 as LOAEL	10	5	5	10	8	8	9	10	3	2	70
22	37	Maynard and Hodge 1949	triuranium octoxide	84.80%	rat	8	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	MOR	MOR	MORT	Mortality	20%		Y	300	Y	15	8480			10	5	5	7	5	10	9	10	3	2	66
23	37	Maynard and Hodge 1949	uranium dioxide	88.20%	rat	13	cntl, 0.5, 2, 20	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	B	MOR	MOR	MORT	Mortality	20%		Y	300	Y	15	8820			10	5	5	7	5	10	9	10	3	2	66
24	37	Maynard and Hodge 1949	uranium dioxide	88.20%	dog	27	cntl, 1, 5, 10	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	MOR	MOR	MORT	Mortality	10						8820			10	5	5	10	5	10	9	10	3	2	69
25	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	5	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	gest to death, M/ F	0	d	IM	F1 F	MOR	MOR	SURV	Survival rate at 21 d		4	NA	NA	NA	NA		4.0	F0 NOAEL 40	10	5	5	10	4	10	9	10	10	7	80
PHYSIOLOGY EFFECT GROUP																																									
1	20	Hao et al 2009	Depleted uranyl nitrate	100%	rat	1	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	gest to 4 mo	0	d	IM	F1 M	PHY	PHY		Bone marrow cell micronuclie rate		4	NA	NA	NA	NA		4.0		10	5	5	10	4	10	4	10	10	7	75
PATHOLOGY EFFECT GROUP																																									
1	44	Raymond-Whish et al. 2007	Uranyl nitrate hexahydrate	47.40%	mouse	1	0, 0.5, 2.5, 12.5, 60	mg UN/L	ADL	DR	30	d	exp to AD	28	d	IM	F	PTH	ORW	ORWT	Kidney wt	0.5	2.5	N	15.3	N	0.005	0.08	0.39	ATSDR 2011 rejected study	10	5	5	5	8	5	4	10	10	7	69
2	37	Maynard and Hodge 1949	uranyl fluoride	77.30%	dog	24	cntl, 0.0002, 0.001, 0.0025, 0.01	g cmpd/kg/d		FD	1	yr		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney	0.0002	0.001					0.155	0.773		10	5	5	10	8	10	4	10	3	2	67
3	29	Lestaevel et al 2009	Depleted uranyl nitrate hexaahydrate	47.40%	rat	1	0, 2	mg DUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	PTH	ORW	ORWT	Brain wt	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	4	10	10	7	71
4	29	Lestaevel et al 2009	Enriched uranyl nitrate hexahydrate	47.40%	rat	2	0, 2	mg EUN/kg/d	ADL	DR	9	mo		NR	NR	IM	M	PTH	ORW	ORWT	Brain wt	2		NA	NA	NA	NA	0.95			10	5	5	10	5	5	4	10	10	7	71
5	47	Souidi et al 2005	Depleted uranyl nitrate hexahydrate	47.40%	rat	1	0, 40	mg UN/L	ADL	DR	9	mo		NR	NR	IM	M	PTH	ORW	ORWR	Kidney, Liver	40		Y	250	Y	1 mg U/ d/rat	1.9			10	5	5	7	5	5	4	10	10	7	68
6	40	Ortega et al 1989a	Uranyl acetate dihydrate	55.90%	rat	1	0, 2, 4, 8, 16	mg UAD/kg/d	ADL	DR	4	wk		NR	NR	IM	M	PTH	HIS	GHIS	Liver, spleen, kidney histology	8	16					4.5	8.9		10	5	5	10	10	5	4	10	7	2	68
7	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	dog	25	cntl, 0.002, 0.01, 0.05	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney	0.01	0.02					6.27	12.54	LOAEL from 30 d study	10	5	5	10	8	10	4	10	3	2	67
8	48	Taulan et al 2004	Uranyl nitrate	47.40%	mouse	1	0, 80, 160	mg UN/L	ADL	DR	4	mo		NR	NR	IM	M	PTH	ORW	ORWT	Kidney wt	160		Y	25-30	N	0.005	12.6			10	5	5	6	5	5	4	10	10	2	62
9	34	Llobet et al 1991	Uranyl acetate dihydrate	55.90%	mouse	1	0, 10, 20, 40, 80	mg UAD/kg.d	ADL	DR	64	d		NR	NR	AD	M	PTH	GRS	BDWT	Adult Body wt	40	80	NA	NA	NA	NA	22.4	44.7		10	5	5	10	8	5	4	3	10	4	64
10	30	Linares et al 2005	Uranyl acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo		NR	NR	SM	M	PTH	GRS	BDWT	Adult Body wt	40		NA	NA	NA	NA	22.4		Reported in ATSDR 2011	10	5	5	10	5	5	4	10	10	7	71
11	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rat	11	0, 0.01, 0.05, 0.1, 0.5, 1, 2	% cmpd in diet	ADL	FD	24	mo		NR	NR	IM	B	PTH	HIS	GHIS	Kidney histology	0.10%	0.50%	Y	300	Y	15	23.7	119	ATSDR 2011 reported as 16.6 and 33 mg/kg/d	10	5	5	7	8	10	4	10	3	2	64
12	37	Maynard and Hodge 1949	uranium tetrachloride	62.70%	rat	2	cntl, 0.2, 0.5, 1, 1.5, 2, 3, 20	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney	0.20%		Y	300	Y	15	62.7			10	5	5	7	5	10	4	10	3	2	61
13	2	Arnault et al. 2008	Uranyl nitrate	100%	mouse	2	0, 1.25, 12.5, 100	mg U/kg/d	ADL	DR	15	wk	euthanized immediately	18	wk	AD	F	PTH	GRS	BDWT	Adult Body wt	100		NA	NA	NA	NA	100		Reported in ATSDR 2011	10	5	5	10	5	5	4	10	10	7	71
14	37	Maynard and Hodge 1949	Uranium acetate	55.90%	rat	6	0, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney histology	0.50%		Y	300	Y	15	140			10	5	5	7	5	10	4	10	3	2	61
15	37	Maynard and Hodge 1949	uranium trioxide	61.60%	rat	5	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney	2.00%		Y	300	Y	15	616			10	5	5	7	5	10	4	10	3	2	61
16	37	Maynard and Hodge 1949	uranium tetrafluoride	75.80%	rat	9	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney	2%	20%	Y	300	Y	15	758	7580		10	5	5	7	8	10	4	10	3	2	64

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
17	37	Maynard and Hodge 1949	triuranium octoxide	84.80%	rat	8	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney	2%		Y	300	Y	15	848			10	5	5	7	5	10	4	10	3	2	61
PATHOLOGY EFFECT GROUP (continued)																																									
18	37	Maynard and Hodge 1949	uranium dioxide	88.20%	rat	7	cntl, 20, 2, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney	20%		Y	300	Y	15	8820			10	5	5	7	5	10	4	10	3	2	61
19	16	Gilman et al 1998 b	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 0.05, 0.20, 0.88,	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	PTH	HIS	GLSN	Liver lesions		0.05	NA	NA	NA	NA		0.05	Reported in ATSDR	10	5	5	10	4	5	4	10	10	4	67
20	15	Gilman et al 1998a	Uranyl nitrate hexahydrate	100%	rat	2	0, 0.06, 0.31, 1.52, 7.54, 36.73	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	PTH	HIS	GLSN	Kidney and liver lesions		0.06	NA	NA	NA	NA		0.06	Reported in ATSDR 2011; F 0.09 mg/kg/d	10	5	5	10	4	5	4	10	10	4	67
21	26	Kelada et al 2008	Uranium acetate dihydrate	100%	rat	1	0, 0.06	mg U/kg/d	DLY	GV	90	d		NR	NR	AD	M	PTH	HIS	GHIS	Brain histology		0.06	NA	NA	NA	NA		0.06		10	5	5	10	4	8	4	10	3	7	66
22	17	Gilman et al 1998c	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 1.36, 40.98	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	PTH	HIS	GLSN	Liver lesions		1.36	NA	NA	NA	NA		1.4	Reported in ATSDR 2011	10	5	5	10	4	5	4	10	10	4	67
23	13	Dominigo et al 1989c	Uranyl acetate dihydrate	55.90%	mouse	1	0, 5, 10, 25, 50	mg UAD/kg/d	DLY	GV	10	d	d 6 to 15 of gest	NR	NR	AD	F	PTH	ORW	ORWT	Adult livr wt		5	NA	NA	NA	NA		2.8		10	5	5	10	4	8	4	10	10	4	70
24	5	Berradi et al 2008	Depleted uranium, NR	100%	rat	1	0, 40	mg DU/L	ADL	DR	9	mo		3	mo	IM	M	PTH	HIS	GHIS	Kedney iron deposits		40	Y	250		1 mg U/ d/rat		4.0		10	4	5	7	4	5	4	10	7	7	63
25	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rabbit	29	0, 0.02, 0.1, 0.5	% cmpd in diet	ADL	FD	30	d		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney histology		0.02%	N					4.7		10	5	5	7	4	10	4	10	3	2	60
26	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	dog	26	0, 0.02, 0.1, 0.2	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney histology		0.02						9.5		10	5	5	10	5	10	4	10	3	2	64
27	37	Maynard and Hodge 1949	uranium peroxide	78.80%	dog	16	cntl, 0.02, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		0.02						15.8		10	5	5	10	4	8	4	10	3	2	61
28	37	Maynard and Hodge 1949	uranyl fluoride	77.30%	rat	1	0, 0.01, 0.05, 0.1, 0.25, 0.5, 0.75, 1, 2,	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney		0.05%	Y	300	Y	15		19.3		10	5	5	7	4	10	4	10	3	2	60
29	18	Goel et al 1979, 1980	Uranyl nitrate	47.40%	rat	1	0, 10	mg UN/d	Alt d	FD	27	d		NR	NR	IM	M	PTH	HIS	GLSN	Liver lesions		10	Y	175-200				23.7		10	5	5	6	5	10	4	10	3	4	62
30	37	Maynard and Hodge 1949	uranium trioxide	61.60%	dog	18	cntl, 0.1, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		0.1						61.6		10	5	5	10	4	8	4	10	3	2	61
31	37	Maynard and Hodge 1949	sodium urnaium oxide	75.10%	dog	19	cntl, 0.1, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		0.1						75.1		10	5	5	10	4	8	4	10	3	2	61
32	37	Maynard and Hodge 1949	ammonium diurante	76.30%	dog	20	cntl, 0.1, 0.5	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		0.1						76.3		10	5	5	10	4	8	4	10	3	2	61
33	37	Maynard and Hodge 1949	uranium peroxide	78.80%	rat	3	cntl, 20, 2, 1, 0.5, 0.25, 0.1	% cmpd in diet	ADL	FD	30	d		NR	NR	JV	B	PTH	HIS	GHIS	Kidney		0.20%	Y	300	Y	15		78.8		10	5	5	7	4	10	4	10	3	2	60
34	37	Maynard and Hodge 1949	uranium tetrafluoride	75.80%	dog	28	cntl, 0.2, 1, 5	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		0.2						151.6		10	5	5	10	5	10	4	10	3	2	64
35	37	Maynard and Hodge 1949	uranium dioxide	88.20%	dog	27	cntl, 1, 5, 10	g cmpd/kg/d	ADL	FD	1	yr		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		1						882		10	5	5	10	5	10	4	10	3	2	64
36	37	Maynard and Hodge 1949	triuranium octoxide	84.80%	dog	22	cntl, 10, 20	g cmpd/kg/d	ADL	FD/ cap	30	d		NR	NR	IM	NR	PTH	HIS	GHIS	Kidney		10						8480		10	5	5	10	4	8	4	10	3	2	61
REPRODUCTION EFFECT GROUP																																									
1	6	Briner and Byrd 2000, Briner and Abboud 2002	Uranium acetate	55.90%	mouse	1	0, 19, 37, 75	mg UAD/L	ADL	DR	55	d	2 wk prior to mate, gest, lact	NR	NR	AD	F	REP	REP	ODVP	% progeny brain wt to body wt	19	37	N	28	N	0.00396	1.5	2.9		10	5	5	5	10	5	10	10	5	4	69
2	14	Feugier et al 2008	Depleted uranium, NR	100%	mouse	1	0, 1.9, 3.9, 6.9	mg DU/kg/d	ADL	DR	49	d		4	wk	IM	F	REP	REP	RHIS	Oocyte quality	1.9	3.9	NA	NA	NA	NA	1.9	3.9	Reported in ATSDR 2011	10	5	5	10	10	5	10	10	10	7	82
3	19	Grignard et al 2008	Depleted uranyl nitrate hexahydrate	100%	rat	1	0, 40	mg DU/L	ADL	DR	9	mo		NR	NR	IM	M	REP	REP	RHIS	Reproductive organ histology	40		Y	250	N	0.012	1.9			10	5	5	6	5	5	10	10	7	7	70
4	19	Grignard et al 2008	Enriched uranium nitrate	100%	rat	2	0, 40	mg EU/L	ADL	DR	9	mo		NR	NR	IM	M	REP	REP	RHIS	Reproductive organ histology	40		Y	250	N	0.012	1.9			10	5	5	6	5	5	10	10	7	7	70
5	42	Paternain et al 1989	Uranyl acetate dihydrate	55.90%	mouse	1	0, 5, 10, 25	mg UAD/kg/d	DLY	GV	60	d	M 60 d prior mate, F 14 d prior mate, gest, lact	NR	NR	AD	B	REP	REP	PROG	Dead young per litter	5	10	NA	NA	NA	NA	2.8	5.6	Reported in ATSDR 2011	10	5	5	10	10	8	10	10	10	4	82
6	12	Domingo et al 1989b	Uranyl acetate dihydrate	55.90%	mouse	2	0, 0.05, 0.5, 5, 50	mg UAD/kg/d	DLY	GV	30	d	d 13 of preg to d 21 of lact	NR	NR	AD	F	REP	REP	PROG	Litter size at 21 d	5	50	NA	NA	NA	NA	2.8	28.0	Reported in ATSDR 2011	10	5	5	10	8	8	10	10	10	4	80

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
REPRODUCTION EFFECT GROUP (continued)																																									
7	24	Houpert et al 2007a	Enriched uranium nitrate	100%	rat	1	0, 40	mg EU/L	ADL	DR	3	mo	M/F exp 3 mo, F exp thru gest/lact	8	wk	IM	B	REP	REP	PROG	Litter size	40		N	230	Y	1 mg U/ d/rat	4.3			10	5	5	6	5	5	10	10	7	7	70
8	1	Albina et al 2005	Uranyl acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo	mated with untrt F	NR	NR	AD	M	REP	REP	PRFM	No pregnant females	10	20	NA	NA	NA	NA	5.6	11.2		10	5	5	10	8	5	10	10	10	7	80
9	30	Linares et al 2005	Uranium acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo		NR	NR	SM	M	REP	REP	PRFM	No pregnant females	10	20	NA	NA	NA	NA	5.6	11.2	Reported in ATSDR 2011	10	5	5	10	10	5	10	10	10	7	82
10	40	Ortega et al 1989a	Uranyl acetate dihydrate	55.90%	rat	1	0, 2, 4, 8, 16	mg UAD/kg/d	ADL	DR	4	wk		NR	NR	IM	M	REP	REP	TEWT	Testes weight	16						8.9			10	5	5	10	5	5	10	10	7	2	69
11	46	Sanchez et al 2006a	Uranyl acetate dihydrate	55.90%	rat	2	0, 40, 80	mg UAD/kg/d	ADL	DR	12	wk	4 wk prior to mate, gest, lact	NR	NR	AD	B	REP	REP	PBEH	Pub behaviour	40	80	NA	NA	NA	NA	22.4	44.7		10	5	5	10	10	5	10	10	10	7	82
12	1	Albina et al 2005	Uranyl acetate dihydrate	55.90%	rat	2	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo	mated with untrt F	NR	NR	AD	M	REP	REP	ODVP	Pup development	40		NA	NA	NA	NA	22.4			10	5	5	10	5	5	10	10	10	7	77
13	33	Linares et al 2008	Uranium acetate dihydrate	55.90%	rat	1	0, 10, 20, 40	mg UAD/kg/d	ADL	DR	3	mo		NR	NR	SM	M	REP	REP	PBEH	F1 offspring behavoir	40		NA	NA	NA	NA	22.4			10	5	5	10	5	5	10	10	7	7	74
14	16	Gilman et al 1998 b	Uranyl nitrate hexahydrate	100%	rabbit	1	0, 0.05, 0.20, 0.88, 4.82, 28.70	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	REP	REP	RHIS	Testes histology	28.7		NA	NA	NA	NA	28.7		Reported in ATSDR 2011; F 43 mg/kg/d	10	5	5	10	5	5	10	10	10	4	74
15	15	Gilman et al 1998a	Uranyl nitrate hexahydrate	100%	rat	2	0, 0.06, 0.31, 1.52, 7.54, 36.73	mg U/kg/d	ADL	DR	91	d		NR	NR	JV	M	REP	REP	RHIS	Testes histology	36.73		NA	NA	NA	NA	36.7		Reported in ATSDR 2011; F 53.6 mg/kg/d	10	5	5	10	5	5	10	10	10	4	74
16	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	1	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	3 wk to 4 mo, M/ F	3	wk	IM	F0 F	REP	REP	PROG	No pups per brood	40		NA	NA	NA	NA	40.0			10	5	5	10	5	10	10	10	10	7	82
17	46	Sanchez et al 2006a	Uranyl acetate dihydrate	55.90%	rat	1	0, 40, 80	mg UAD/kg/d	ADL	DR	6	wk	4 wk prior to mate, gest, lact	NR	NR	AD	B	REP	REP	PROG	No viable implants per litter	80		NA	NA	NA	NA	44.7			10	5	5	10	5	5	10	10	10	7	77
18	12	Domingo et al 1989b	Uranyl acetate dihydrate	55.90%	mouse	2	0, 0.05, 0.5, 5, 50	mg UAD/kg/d	DLY	GV	30	d	d 13 of preg to d 21 of lact	NR	NR	AD	F	REP	REP	OTHR	Liver wt of progeny		0.05	NA	NA	NA	NA		0.03		10	5	5	10	4	8	10	10	10	4	76
19	44	Raymond-Whish et al. 2007	Uranyl nitrate hexahydrate	47.40%	mouse	2	0, 0.5, 2.5, 12.5, 60	mg UN/L	ADL	DR	21	d	gest exp to dams; pups euthanized at time of birth	48	d	AD	F	REP	REP	RHIS	No primoridal follicle in pups		0.5	N	15.3	N	0.005		0.08	ATSDR 2011 rejected study; considered anomanously low; non-dose depedent	10	5	5	5	4	5	10	10	7	7	68
20	2	Arnault et al. 2008	Uranium nitrate	100%	mouse	1	0, 1.25, 12.5	mg U/kg/d	ADL	DR	15	wk	exp to dams	7.5	mo	AD	F	REP	REP	RHIS	Pup Follicle size		1.25	NA	NA	NA	NA		1.3	Reported in ATSDR 2011	10	5	5	10	4	5	10	10	10	7	76
21	2	Arnault et al. 2008	Uranium nitrate	100%	mouse	2	0, 1.25, 12.5, 100	mg U/kg/d	ADL	DR	15	wk	F euthanized immediately	18	wk	AD	F	REP	REP	RHIS	Follicle size		1.25	NA	NA	NA	NA		1.3	Reported in ATSDR 2011	10	5	5	10	4	5	10	10	10	7	76
22	27	Kundt et al 2009	Uranyl nitrate	100%	mouse	1	0, 2.5, 5 10	mg U/kg/d	ADL	DR	40	d	exp IM to AD	21	d	IM	F	REP	REP	RHIS	Oocyte dysmorphism		2.5	NA	NA	NA	NA		2.5	Reported in ATSDR 2011, non-dose dependent	10	5	5	10		5	10	10	10	2	67
23	13	Dominigo et al 1989c	Uranyl acetate dihydrate	55.90%	mouse	1	0, 5, 10, 25, 50	mg UAD/kg/d	DLY	GV	10	d	d 6 to 15 of gest	NR	NR	AD	F	REP	REP	PRWT	Fetus weight		5	NA	NA	NA	NA		2.8		10	5	5	10	4	8	10	10	10	4	76
24	20	Hao et al 2009	Depleted uranyl nitrate	100%	rat	1	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	gest to 4 mo	0	d	IM	F1 M	REP	REP	RHIS	Sperm abnorm rate		4	NA	NA	NA	NA		4.0		10	5	5	10	4	10	10	10	10	7	81
25	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	3	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	3 wk to 4 mo, M/F	3	wk	IM	F0 M	REP	REP	TERA	Sex hormones in serum		4	NA	NA	NA	NA		4.0		10	5	5	10	4	10	10	10	10	7	81
26	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	4	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	gest to death, M/F	0	d	IM	F1 F	REP	REP	PROG	No of pups per brood		4	NA	NA	NA	NA		4.0	F0 NOAEL 40 mg/kg/d	10	5	5	10	4	10	10	10	10	7	81
27	21	Hao et al 2012	Depleted uranyl nitrate	100%	rat	6	0, 4, 40	mg DU/kg/d	ADL	FD	4	mo	gest to death, M/ F	0	d	IM	F1 M	REP	REP	TERA	Sex hormones in serum		4	NA	NA	NA	NA		4.0	F0 LOAEL 4 mg/kg/d	10	5	5	10	4	10	10	10	10	7	81
28	24	Houpert et al 2007a	Enriched uranyl nitrate	100%	rat	1	0, 40	mg EU/L	ADL	DR	3	mo	M/F exp 3 mo, F exp thru gest/lact	8	wk	IM	B	REP	REP	PBEH	F1 offspring behavoir		40	N	230	Y	1 mg U/ d/rat		4.3	Reported in ATSDR 2011	10	5	5	6	4	5	10	10	7	7	69
29	34	Llobet et al 1991	Uranyl acetate dihydrate	55.90%	mouse	1	0, 10, 20, 40, 80	mg UAD/kg/d	ADL	DR	64	d		NR	NR	AD	M	REP	REP	PRFM	No pregnant females		10	NA	NA	NA	NA		5.6	Reported in ATSDR 2011	10	5	5	10	4	5	10	3	10	4	66
30	36	Malenchenko et al 1978	Uranyl nitrate	44.70%	rat	1	0, 0.1	% UN in DR	ADL	DR	4	mo		NR	NR	AD	NR	REP	REP	ORWT	Reduced testis wt		0.10%	N	250	N	15		27		10	5	5	5	4	5	10	10	7	2	63
31	39	Miller et al 2010	Depleted uranyl nitrate	100	mouse	1	0, 50	mg DU/L	ADL	DR	2	mo		NR	NR	AD	M	REP	REP	PROG	Litter size		50	N	15.3	Y	1 mg U/ d/mouse		65.4		10	5	5	7	4	5	10	3	10	7	66
32	39	Miller et al 2010	Enriched uranyl nitrate	100	mouse	2	0, 50	mg EU/L	ADL	DR	2	mo		NR	NR	AD	M	REP	REP	PROG	Litter size		50	N	15.3	Y	1 mg U/ d/mouse		65.4		10	5	5	7	4	5	10	3	10	7	66
33	37	Maynard and Hodge 1949	Uranyl nitrate hexahydrate	47.40%	rat	11	0, 1	% cmpd in diet	ADL	FD	195	d		NR	NR	IM	B	REP	REP	PROG	No litters/ young per litter		2.00%	Y	300	Y	15		474		10	5	5	7	4	10	10	10	3	2	66

Table 1. Toxicity data used in the derivation of a mammalian reference value for uranium. (Continued)

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Referance #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in g	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
REJECTED																																									
1	7	Briner 2002	Depleted uranium acetate	55.90%	rat	1	0, 75	mg DUAD/L	ADL	DR	6	mo		NR	NR	AD	M	BEH	BEH	NMVM	No of movements		75	Y	500	N	0.053		4.4	F LOAEL 4.6 mg/kg/d	10	5	5	6	4	5	4	10	5	4	58
2	7	Briner 2002	Depleted uranium acetate	55.90%	rat	1	0, 75	mg DUAD/L	ADL	DR	6	mo		NR	NR	AD	M	PTH	GRS	BDWT	Body weight	75		Y	500	N	0.053	4.4		F LOAEL 4.6 mg/kg/d	10	5	5	6	5	5	4	10	5	4	59
3	8	Briner and Davis 2002	Uranium acetate	55.90%	mouse	1	0, 19, 37, 75	mg UAD/L	ADL	DR	2	wk		NR	NR	AD	M	BIO	CHM		Inceased Lipd oxidation	19	37	N	32	N	0.004	1.5	2.9		10	5	5	5	10	5	1	3	5	4	53
4	8	Briner and Davis 2002	Uranium acetate	55.90%	mouse	1	0, 19, 37, 75	mg UAD/L	ADL	DR	2	wk		NR	NR	AD	M	BEH	BEH	NMVM	More active rearing actions		19	N	32	N	0.004		1.5		10	5	5	5	4	5	4	3	5	4	50
5	36	Malenchenko et al 1978	Uranyl nitrate	44.70%	rat	1	0, 0.1	% UN in DR	ADL	DR	4	mo		NR	NR	AD	NR	PTH	ORW	ORWT	Increased spleen weight		0.10%	N	250	N	15		27		10	5	5	5	4	5	4	10	7	2	57
6	38	McDonald-Taylor et al 1992, 1997	Uranyl nitrate hexahydrate	47.40%	rabbit	1	0, 24, 600	mg UN/L	ADL	DR	91	d		NR	NR	JV	M	PTH	HIS	GHIS	Kidney		24	N	2860	N	0.255		1.0		10	5	5	5	4	5	4	10	7	4	59
7	45	Rouas et al 2011	Depleted uranyl nitrate	47.40%	rat	1	0, 40	mg UN/L	ADL	DR	9	mo		NR	NR	IM	M	BEH	FDB	CAIN/ WCON	Caloric intake/water consumption	40		Y	250	Y	1 mg UN/ d/rat	1.1			10	5	5	7	5	5	4	10	5	2	58
8	48	Taulan et al 2004	Uranyl nitrate	47.40%	mouse	1	0, 80, 160	mg UN/L	ADL	DR	4	mo		NR	NR	IM	M	BEH	FDB	CAIN/ WCON	Caloric intake/water consumption	160		Y	25-30	N	0.005	12.6			10	5	5	6	5	5	4	10	5	2	57

Columns not presented : Rationale
Wet Weight Reported? : No wet weight was reported for any paper
Percent Moisture : No wet weight was reported for any paper
Control Type : Valid vehicle application control was used in all papers
Test Location : Laboratory the location for all papers
Endpoint Number : Replaced by endpoint description
Response Site : Replaced by endpoint description
Method of Analysis : All unmeasured
conc/doses : Redundant to dose/conc column

Table 2. Toxicity data used in the derivation of an avian toxicity reference value for uranium.

Referance			Exposure																					Conversion to mg/kg/d				Result			Data Evaluation Score										
Result #	Reference #	Reference	Chemical Form	Administered amount (MW%)	Test Species	Phase #	Conc/Dose	Study Conc/Dose Units (Units for study NOAEL and LOAEL)	Application Frequency	Route of Exposure	Exposure Duration	Duration Units	Duration comments	Age	Age Units	Lifestage	Sex	Effect Group	Effect Type	Effect Measure	Endpoint Description	Study NOAEL (Conc/ Dose units)	Study LOAEL (Conc/ Dose units)	Body weight reported?	Body weight in kg	Ingestion Rate Reported?	Ingestion Rate in kg/d or L/d	NOAEL Dose (mg/kg/d)	LOAEL Dose (mg/kg/d)	NOAEL/ LOAEL Comments	Data Source	Chemical form	Test Concentration	Dose Quantification	Dose Range	Dose Route	Endpoint	Exposure Duration	Statistical Analysis	Test Conditions	Total
Subchronic, oral studies																																									
1	1	Haseltine and Sileo 1983	Uranium, elemental (powdered)	100%	duck, mallard	1	0, 25, 100, 400, 1600	ppm U	ADL	FD	6	wk		9	mo	AD	B	MOR	MOR	GMOR	Mortality	1600		Y	1.25	N	0.125	160		Calculations as in Sample 1996	10	5	5	5	5	10	9	6	8	2	65
2	1	Haseltine and Sileo 1983	Uranium, elemental (powdered)	100%	duck, mallard	1	0, 25, 100, 400, 1600	ppm U	ADL	FD	6	wk		9	mo	AD	B	PTH	GRS	BDWT	Body wt	1600		Y	1.25	N	0.125	160		Calculations as in Sample 1996	10	5	5	5	5	10	4	6	8	2	60
3	1	Haseltine and Sileo 1983	Uranium, elemental (powdered)	100%	duck, mallard	1	0, 25, 100, 400, 1600	ppm U	ADL	FD	6	wk		9	mo	AD	B	PTH	ORW	ORWT	Kidney and Liver wt	1600		Y	1.25	N	0.125	160		Calculations as in Sample 1996	10	5	5	5	5	10	4	6	8	2	60
4	1	Haseltine and Sileo 1983	Uranium, elemental (powdered)	100%	duck, mallard	1	0, 25, 100, 400, 1600	ppm U	ADL	FD	6	wk		9	mo	AD	B	PTH	HIS	GHIS	Kideny lesions	1600		Y	1.25	N	0.125	160		Calculations as in Sample 1996	10	5	5	5	5	10	4	6	8	2	60
5	1	Haseltine and Sileo 1983	Uranium, elemental (powdered)	100%	duck, mallard	1	0, 25, 100, 400, 1600	ppm U	ADL	FD	6	wk		9	mo	AD	B	BIO	CHM		PCV, hemoglobin, ALAD, uric acid, AST and ATT	1600		Y	1.25	N	0.125	160		Calculations as in Sample 1996	10	5	5	5	5	10	1	6	8	2	57
Acute, non-oral studies																																									
1	2	Harvey et al 1986a	Uranyl nitrate hexahydrate	47.40%	chicks, Leghorn	1	0, 70, 100, 130, 160, 190, 220, 280, 310, 340, 370, 400, 430, 460	mg UN/kg body wt	Single	SC	NA	NA	Group mortality monitored for 7 d	4	wk	JV	B	MOR	MOR	MORT	Mortality	130	160	NA	NA	NA	NA	61.6	75.8	NOAEL/LOAEL units are mg/kg. LD50 reported as 235 mg UN/kg (110 mg U/kg) and reported to be 100 to 200 times the 14 to 21 d LD50 for rats	10	5	5	10	10	0	9	0	8	4	61

Appendix A

Appendix A

List of Tables

Table A-1. Receptors from U. S. EPA (2003a) used in the literature search.

Avian Receptors		
chicken	**quail**	**duck**
duckling	**ducks**	**mallard**
Japanese quail	**coturnix**	**gallus domesticus**
platyrhyn*	**anas**	**songbird**
bobwhite	**waterbird**	**waterfowl**
aves	**avain**	**bird**
Laboratory Mammals		
rat	**rats**	**mouse**
mice	**hamster**	**guinea pig**
monkey	**rabbit**	
Wild Mammals		
Didelphidae	**Soricidae**	**Talpidae**
Dasypodidae	**Ochotonidae**	**Leporidae**
Aplodontidae	**Sciuridae**	**Geomyidae**
Heteromyidae	**Castoridae**	**Arvicolinae**
Dipodidae	**Erethizontidae**	**Myocastoridae**
Canidae	**Ursidae**	**Procyonidae**
Mustelidae	**Felidae**	**Equidae**
Suidae	**Dicotylidae**	**Cervidae**
Antilocapridae	**Bovidae**	**Sigmodontinae**
Harvet mice	**Harvest mouse**	**Microtus**
Peromyscus	**Reithrodontomys**	**Onychomys**
Sigmodon	**vole**	**lemming**
cat	**dog**	**bear**
opossum	**beaver**	**weasel**
skunk	**marten**	**badger**
ferret	**mink**	

Notes:

* **Denotes the term is truncated.**

Table A-2. Rejection codes from U. S. EPA (2007d) used in evaluating uranium toxicity literature.

Code	Description
Abstract	Abstract: Abstracts of journal publications or conference presentations.
Acu	Acute Studies: Single oral dose or exposure of three days or less.
Alt	Altered Receptor: Studies that describe the effects of the contaminant on surgically-altered or chemically-modified receptors.
Bio Acc	Bioaccumulation Survey: Studies reporting the measurement of the concentrations of the contaminant in tissues.
Carcin	Carcinogenicity Studies: Studies that report data only for carcinogenic endpoints such as tumor induction. Papers that also report systemic toxicity data were retained and coded for the appropriate endpoints.
Diss	Dissertations.
Dup	Duplicate Data: Studies reporting results that are duplicated in a separate publication. The publication with the earlier year was used.
Fate	Chemical Fate/Metabolism: Studies reporting on what happens to the contaminant rather than what happens to the organism. Studies describing the intermediary metabolism of the contaminant without the description of adverse effects.
FL	Foreign Language: Studies in languages other than English.
Gene	Gene: Studies of genotoxicity (chromosomal aberrations and mutagenicity).
HHE	Human Health: Studies with human subjects.
IMM	Immunology: Studies on effects of contaminants on immunological endpoints.
In vit	In Vitro: In vitro studies, including exposure of cell cultures, excised tissues and/or excised organs.
Invert	Invertebrate: Studies that investigate the effects of contaminants on terrestrial invertebrates.
Meth	Methods: Studies reporting methods or methods development without usable toxicity results for specific endpoints.
Mix	Mixture: Studies that report data for combinations of single toxicants.
Model	Model: Studies reporting the use of existing data for modeling, i.e., no new organism toxicity data are reported.
No Control	No Control: Studies which lack a valid control.
No Oral	No Oral: Studies using non-oral routes of contaminant administration including intraperitoneal injection, other injection, inhalation and dermal exposures.
Not Prim	Not Primary: Papers that are not the original compilation and/or publication of the experimental data.
Nut	Nutrition: Studies examining the best or minimum level of chemical in the diet.
Phys	Physiology Studies: Physiology studies where adverse effects are not associated with exposure to the contaminant.
Rev	Review: Studies in which the data reported in the article are not primary data from research conducted by the author. Publication was reviewed to identify relevant literature.
Surv	Survey: Studies reporting the toxicity of a contaminant in the field over a period of time. Often neither duration or an exposure concentration is reported.
Unrel	Unrelated: Studies that are unrelated to the contaminant exposure and response and/or the receptor groups of interest.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium.

Reject Code	Reference
Rev	Abu-Qare, A. W. and M. B. Abou-Donia (2002). "Depleted uranium - the growing concern." Journal of Applied Toxicology 22(3): 149-152.
Surv	Anke, M., O. Seeber, et al. (2009). "Uranium transfer in the food chain from soil to plants, animals and man." Chemie Der Erde-Geochemistry 69: 75-90.
No Oral	Ansborlo, E., J. Chalabreysse, et al. (1990). "IN-VITRO SOLUBILITY OF URANIUM TETRAFLUORIDE WITH OXIDIZING MEDIUM COMPARED WITH IN-VIVO SOLUBILITY IN RATS." Int J Radiat Biol 58(4): 681-690.
No Oral	Arfsten, D. P., D. J. Schaeffer, et al. (2006). "Evaluation of the effect of implanted depleted uranium on male reproductive success, sperm concentration, and sperm velocity." Environ Res 100(2): 205-215.
Rev	Arfsten, D. P., K. R. Still, et al. 2001. A review of the effects of uranium and depleted uranium exposure on reproduction and fetal development. Toxicology and Industrial Health 17(5-10): 180-191.
No Oral	Arfsten, D. P., K. R. Still, et al. (2009). "Two-generation reproductive toxicity study of implanted depleted uranium (DU) in CD rats." J Toxicol Environ Health A 72(6): 410-427.
Bio acc	Arruda-Neto, J. D. T., M. V. M. Guevara, et al. (2004). "Long-term accumulation of uranium in bones of Wistar rats as a function of intake dosages." Radiation Protection Dosimetry 112(3): 385-393.
Gene	Arutyunyan, S. K. and V. A. Shevchenko (1986). "[Genetic screening of uranyl
Rev	Arzuaga, X., S. H. Rieth, et al. 2010. Renal effects of exposure to natural and depleted uranium: a review of the epidemiologic and experimental data. J Toxicol Environ Health B Crit Rev 13(7-8): 527-545.
Not Prim	Aschner, M. (2002). "Blood-Brain Barrier Transport of Uranium." Govt Reports Announcements & Index(19): 18.
No Oral	Aschner, M. (2005). "Blood-Brain Barrier Transport of Uranium." Govt Reports
Rev	ATSDR. 2011. Draft Toxicological Profile for Uranium. Agency for Toxic Substances and Disease Registry. Division of Toxicology and Environmental Medicine/Applied Toxicology Branch. Atlanta, Georgia. May 2011.
Acu	Austin, J. H. and A. B. Eisenbrey (1911). "EXPERIMENTAL ACUTE NEPHRITIS: THE ELIMINATION OF NITROGEN AND CHLORIDES AS COMPARED WITH THAT OF PHENOLSULPHONEPHTHALEIN." J Exp Med 14(4): 366-376.
Unrel	Balazs, T. (1974). "Development of tissue resistance to toxic effects of chemicals." Toxicology 2(3): 247-255.
Acu	Balazs, T., A. Hatch, et al. (1963). "Renal Tests In Toxicity Studies On Rats." Toxicology and Applied Pharmacology 5(5): 661-674.
Acu; No Oral	Banday, A. A., S. Priyamvada, et al. (2008). "Effect of uranyl nitrate on enzymes of carbohydrate metabolism and brush border membrane in different kidney tissues." Food and Chemical Toxicology 46(6): 2080-2088.
No Oral	Barber, D. S., S. K. Hancock, et al. (2006). "Neurological Effects Of Chronic Uranium And Stress Exposure." Toxicol Sci 90(1-S): 369.
Acu; No Oral	Barber, D., S. Hancock, et al. (2005). "Neurological Effects Of Acute Uranium Exposure." Toxicol Sci 84(1-S): 123.
Acu	Basinger, M. A., R. L. Forti, et al. (1983). "Phenolic Chelating Agents As Antidotes For Acute Uranyl Acetate Intoxication In Mice." Journal of Toxicology and Environmental Health 11(2): 237-246.
HHE; Model; Acu	Bast, C., G. Rusch, et al. (2004). "Acute Exposure Guideline Levels (AEGLs) For Uranium Hexafluoride." Toxicologist 78(1-S): 148-149.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Acu	Bencosme, S. A., R. S. Stone, et al. (1960). "Acute Tubular And Glomerular Lesions In Rat Kidneys After Uranium Injury." AMA Archives of Pathology 64(3): 470-476.
No Oral	Benson, K. A. (1998). "Evaluation of the Health Risks of Embedded Depleted Uranium (DU) shrapnel on Pregnancy and Offspring Development." Govt Reports Announcements & Index(06): 36.
Fate	Bentley, K. W., J. H. Wyatt, et al. (1982). "URANIUM AND PLUTONIUM IN HAIR AS AN INDICATOR OF BODY BURDEN IN MICE OF DIFFERENT AGE AND SEX." Bulletin of Environmental Contamination and Toxicology 28(6): 691-696.
Carcin	Berke, H. L. and M. J. Palazzolo (1974). "THE BLASTOGENIC EFFECT OF URANYL NITRATE ON THE PERIPHERAL LYMPHOCYTE OF THE RAT." American Industrial Hygiene Association Journal 35(4): 207-217.
Abstract	Berradi, H., L. Grandcolas, et al. 2007. Long-term ingestion of depleted uranium via drinking water markedly modifies rat iron metabolism. Annals of Nutrition and Metabolism 51: 398-398.
No Oral	Bienvenu, P., C. Nofre, et al. (1963). "General Comparative Toxicology Of Metallic Ions. Relation To Their Periodic Classification." Academie Des Sciences Comptes Rendus 256(10): 1043-1044.
Acu:	Blantz, R. C., J. C. Pelayo, et al. (1985). "Functional basis for the glomerular alterations in uranyl nitrate acute renal failure." Kidney International 28(5): 733-743.
Rev	Bosshard, E., B. Zimmerli, et al. 1992. Uranium in the diet: Risk assessment of its nephro-and radiotoxicity. Chemosphere 24(3): 309-321.
Rev	Briner, W. 2010. The Toxicity of Depleted Uranium. International Journal of Environmental Research and Public Health 7(1): 303-313.
Rev	Brugge, D. and V. Buchner. 2011. Health effects of uranium: new research findings. Reviews on Environmental Health 26(4): 231-249.
Rev	Brugge, D., J.L. de Lemos, and B. Oldmixon. 2005. Exposure pathways and health effects associated with chemical and radiological toxicity of natural uranium: a review. Rev Environ Health 20:177-93.
Mix	Bulger, R. E. (1986). "Renal damage caused by heavy metals." Toxicologic Pathology 14(1): 58-65.
Abstract	Cabrini, R. L., M. B. Gulielmotti, et al. (1984). "Prevention of the toxic effect of uranium on bone formation by tetracycline." Acta Odontol Latinoam 1(2): 1985).
Abstract; Model	Castoldi, A. F., P. Ferrari, et al. (2009). "EFSA's risk assessment of uranium in foodstuffs and water." Toxicology Letters (Shannon) 189(Sp. Iss. SI): S230-S231.
Model	Cheng, J., I. Hlohowskyj and C. L. Tsao. 2004. Ecological Risk Assessment of Radiological Exposure to Depleted Uranium in Soils at a Weapons Testing Facility. Soil and Sediment Contamination 13:579-595.
Bio acc; Surv	Cloutier, N. R., F. V. Clulow, et al. (1985). "Metal copper nickel iron cobalt zinc lead and radium-226 levels in meadow voles microtus-pennsylvanicus living on nickel and uranium mine tailings in ontario canada environmental and tissue levels." Environ Pollut Ser B Chem Phys 10(1): 19-46.
Bio acc; Surv	Cloutier, N. R., F. V. Clulow, et al. (1986). "Metal copper nickel iron cobalt zinc lead and radium-226 levels in tissues of meadow voles microtus-pennsylvanicus living on nickel and uranium mine tailings in ontario canada site sex age and season effects with calculation of average skeletal radiation dose." Environ Pollut Ser a Ecol Biol 41(4): 295-314.
Surv; Fate	Clulow, F. V., M. A. Mirka, et al. (1991). "Radium-226 and other radionuclides in water, vegetation, and tissues of beavers (Castor canadensis) from a watershed containing uranium tailings near Elliot Lake, Canada." Environmental Pollution 69(4): 277-310.
Surv	Clulow, F. V., N. K. Dave, et al. (1996). "U- and Th-series radionuclides in snowshoe hare (Lepus americanus) taken near U mill tailings close to Elliot Lake, Ontario, Canada." Environmental Pollution 94(3): 273-281.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Surv; Unrel	Clulow, F. V., T. P. Lim, et al. (1992). "RA-226 LEVELS AND CONCENTRATION RATIOS BETWEEN WATER, VEGETATION, AND TISSUES OF RUFFED GROUSE (BONASA-UMBELLUS) FROM A WATERSHED WITH URANIUM TAILINGS NEAR ELLIOT LAKE, CANADA." Environmental Pollution 77(1): 39-50.
Fate	Cooper, J. R., G. N. Stradling, et al. (1982). "The behaviour of uranium-233 oxide and uranyl-233 nitrate in rats." Int J Radiat Biol Relat Stud Phys Chem Med 41(4): 421-433.
Rev	Craft, E. S., A. W. Abu-Qare, et al. 2004. Depleted and natural uranium: chemistry and toxicological effects. Journal of Toxicology and Environmental Health-Part B-Critical Reviews 7(4): 297-317.
No Oral	Cross, F. T., R. F. Palmer, et al. (1981). "DEVELOPMENT OF LESIONS IN SYRIAN GOLDEN-HAMSTERS FOLLOWING EXPOSURE TO RADON DAUGHTERS AND URANIUM ORE DUST." Health Physics 41(1): 135-153.
No Oral	Dahl, L. K. (1953). "The stages in calcification of the rat kidney after the administration of uranium nitrate." J Exp Med 97(5): 681-694.
No Oral	Damon, E. G., A. F. Eidson, et al. (1986). "Effect of acclimation to caging on nephrotoxic response of rats to uranium." Laboratory Animal Science 36(1): 24-27.
No Oral; Fate	De Rey, B. M., H. E. Lanfranchi, et al. (1983). "Percutaneous absorption of uranium compounds." Environmental Research 30(2): 480-491.
Acu	Delagarza, M. L. G. and B. M. Derey (1984). "GROWTH-RATE ALTERATIONS OF THE RAT CENTRAL INCISOR PRODUCED BY URANYL-NITRATE." Journal of Dental Research 63(4): 607-607.
Fate; Phys	Diamond, G. L. and R. K. Zalups (1998). "Understanding renal toxicity of heavy metals." Toxicologic Pathology 26(1): 92-103.
No Oral	Diamond, G. L., P. E. Morrow, et al. (1989). "REVERSIBLE URANYL FLUORIDE NEPHROTOXICITY IN THE LONG EVANS RAT." Fundamental and Applied Toxicology 13(1): 65-78.
Rev	Domingo JL. 1995. Chemical toxicity of uranium. Toxicol Ecotoxicol News 2:74–8.
Rev	Domingo, J. L. 1994. Metal-induced developmental toxicity in mammals: a review. Journal of Toxicology and Environmental Health 42(2): 123-141.
Abstract	Domingo, J. L., A. Ortega, et al. 1989a. Developmental effects on mice after prenatal and postnatal exposure to uranium. Toxicologist 9(1): 272.
Acu	Domingo, J. L., J. M. Llobet, et al. (1987). "Acute Toxicity of Uranium in Rats and Mice." Bulletin of Environmental Contamination and Toxicology 39(1): 168-174.
Rev	Domingo, J.L., 2001. Reproductive and developmental toxicity of natural and depleted uranium: a review. Reproductive Toxicology 15, 603–609.
Bio acc	Donnadieu-Claraz, M., M. Bonnehorgne, et al. 2007. Chronic exposure to uranium leads to iron accumulation in rat kidney cells. Radiation Research 167(4): 454-464.
Surv	Dowdall, M., S. Gerland, et al. (2003). "Gamma-emitting natural and anthropogenic radionuclides in the terrestrial environment of Kongsfjord, Svalbard." Science of the Total Environment 305(1-3): 229-240.
Imm	Dublineau, I., L. Grandcolas, et al. 2007. Modifications of inflammatory pathways in rat intestine following chronic ingestion of depleted uranium. Toxicological Sciences 98(2): 458-468.
Bio acc; In vit	Dublineau, I., S. Grison, et al. (2005). "Absorption of uranium through the entire gastrointestinal tract of the rat." Int J Radiat Biol 81(6): 473-482.
No Oral	Dublineau, I., S. Grison, et al. (2006). "Absorption, accumulation and biological effects of depleted uranium in Peyer's patches of rats." Toxicology 227(3): 227-239.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Acu; No Oral	Dublineau, I., S. Grison, et al. (2006). "Short-term effects of depleted uranium on immune status in rat intestine." Journal of Toxicology and Environmental Health-Part a-Current Issues 69(17): 1613-1628.
Bio acc; Fate	Durakovic, A. (1999). "Medical effects of internal contamination with uranium." Croatian Medical Journal 40(1): 49-66.
Rev	Durbin, P.A. and M. E. Wrenn. 1975. Metabolism and effects of uranium in animals, vol 93. Energy Research and Development Administration, Arlington, VA, pp. 67-129.
Not Prim	Dyer, C. H. (2007). Estrogenic activity of uranium in vitro and in vivo. Crisp Data Base National Institutes of Health. Arizona.
Abstract	Eidson, A. F., W. C. J. Griffith, et al. (1989). "A model for scaling the results of uranium excretion rate studies in beagle dogs to man." 26th Hanford Life Sciences Symposium on Modeling for Scaling to Man: Biology, Dosimetry, and Response. Health Phys 57(SUPPL. 1): 199-210.
No Oral; Fate	Ellender, M., J. W. Haines, et al. (1995). "The distribution and retention of plutonium, americium and uranium in CBA/H mice." Hum Exp Toxicol 14(1): 38-48.
Not Prim	Evans, H. L. and S. A. Daniel (1994). Behavioral toxicology from the lab to the natural environment. Chang, L. W. (Ed.). Neurological Disease and Therapy, 26. Principles of Neurotoxicology. Xviii+800p. Marcel Dekker, Inc.: New York, New York, USA; Basel, Switzerland. Isbn 0-8247-8836-2.; 0 (0). 1994. 443-474.
Model	Fan, M., Tepwitoon Thongsri, Lisa Axe and Trevor A. Tyson. 2005. Using a probabilistic approach in an ecological risk assessment simulation tool: test case for depleted uranium (DU). Chemosphere 60: 111–125.
Fate	Feldman, I., J. Jones, and R. Cross. 1967. Chelation of uranyl ions adenine nucleotides. J. Am. Chem. Soc. 89:49-55.
Rev	Fisher, RD. 1987. Toxicology of uranium: a review. In: Seiler S (ed) Handbook on the Toxicity of Inorganic Compounds. Industrial Engineering Series. Marcel Dekker, New York.
Acu	Flamenbaum, W., M. L. Huddleston, et al. (1974). "URANYL NITRATE INDUCED ACUTE RENAL FAILURE IN THE RAT MICRO PUNCTURE AND RENAL HEMODYNAMIC STUDIES." Kidney International 6(6): 408-418.
Acu	Flamenbaum, W., R. J. Hamburger, et al. (1976). "THE INITIATION PHASE OF EXPERIMENTAL ACUTE RENAL FAILURE AN EVALUATION OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE IN THE RAT." Kidney International Supplement 6: S115-S122.
In vit	Florent, C., L. Tekaya, et al. (2001). "Analytical microscopy observations of rat enterocytes after oral administration of soluble salts of lanthanides, actinides and elements of group III-A of the periodic chart." Cellular and Molecular Biology 47(3): 419-425.
No Oral	Foulkes, E. C. 1971. Glomerular filtration and renal plasma flow in uranium-poisoned rabbits. Toxicol. App. Pharmacol. 20:380-385.
Rev; Model	Garten, C. T. J. (1978). "A REVIEW OF PARAMETER VALUES USED TO ASSESS THE TRANSPORT OF PLUTONIUM URANIUM AND THORIUM IN TERRESTRIAL FOOD CHAINS." Environmental Research 17(3): 437-452.
Fate; Acu	Gartland, K. P., B. C. Sweatman, et al. (1991). Proton nuclear magnetic resonance urinalysis studies on the biochemical effects of a nephrotoxic dose of uranyl nitrate in the fischer 344 rat. Bach, P. H., Et Al. (Ed.). Nephrotoxicity: Mechanisms, Early Diagnosis, and Therapeutic Management; Fourth International Symposium on Nephrotoxicity, Guilford, England, Uk, 1989. Xiii+586p. Marcel Dekker, Inc.: New York, New York, USA; Basel, Switzerland. Illus. Isbn 0-8247-8366-2.; 0 (0). 1991. 525-530.
Fate	Gawlik, Z., H. Molak-Olczakowa, et al. (1976). "Renal glomerular and tubular lesions in rabbits treated with uranyl nitrate." Pol Med Sci Hist Bull 15(1): 19-31.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Rev	Geras'kin, S. A., Evseeva, T. I. , Belykh, E.S., Majstrenko, T.A., Michalik, B., Anatoliy, T.I. (2007). "Effects on non-human species inhabitating areas with enhanced level of natural radioactivity in the north of Russia: a review." Journal of Environmental Radioactivity 94: 151-182.
Mix; No Oral	Gies, R. A., F. T. Cross, et al. (1993). "A histopathological comparison of mixed exposures to radon progeny and uranium ore dust in rats." Health Physics 64(SUPPL. 6): S53.
Unrel	Gil'iano, N., O. V. Malinovskii, et al. (1990). "[The induction of hepatocyte polyploidization in rats of various ages by ionizing irradiation with different LETs]." Radiobiologiia 30(2): 194-198.
In vit:	Goldman, M., A. Yaari, et al. (2006). "Nephrotoxicity of uranyl acetate: effect on rat kidney brush border membrane vesicles." Archives of Toxicology 80(7): 387-393.
Mix; Abstract:	Grandcolas, L., C. Rouas, et al. (2009). "Impact of chronic exposure with low dose of depleted uranium on rats treated with different acetaminophen doses." Toxicology Letters (Shannon) 189(Sp. Iss. SI): S112-S113.
Surv; Unrel	Grashchenko, S. M., Z. G. Gritchenko, et al. (1997). "Distribution of natural radionuclides of the uranium and thorium series in the course of treatment of artesian water for drinking water supply." Radiochemistry 39(5): 477-480.
Abstract	Grison, S., L. Grandcolas, et al. (2008). "Impact of a chronic ingestion of uranium at low level on plasma profile in rats." Toxicology Letters (Shannon) 180(Suppl. 1): S183.
Gene	Gueguen, Y., F. Paquet, et al. (2005). Effects of chronic contamination with depleted uranium on xenobiotic biotransformation enzymes in the rat. 40128 Bologna, Medimond S R L.
Mix	Gueguen, Y., L. Grandcolas, et al. (2007). "Effect of acetaminophen administration to rats chronically exposed to depleted uranium." Toxicology 229(1-2): 62-72.
Acu	Guglielmotti, M. B., A. M. Ubios, et al. (1984). "Effects of acute intoxication with uranyl nitrate on bone formation." Experientia 40(5): 474-476.
Acu	Haley, D. (1978). "A SCANNING ELECTRON MICROSCOPE STUDY OF THE URANYL NITRATE MODEL OF ACUTE RENAL FAILURE." Anatomical Record 190(2): 411-412.
Acu	Haley, D. P. (1982). "MORPHOLOGIC CHANGES IN URANYL NITRATE INDUCED ACUTE RENAL FAILURE IN SALINE DRINKING AND WATER DRINKING RATS." Laboratory Investigation 46(2): 196-208.
Rev	Hamilton, E. I. 2001. Depleted uranium (DU): a holistic consideration of DU and related matters. Sci Total Environ 281:5-21.
Bio acc	Harrison, J. D. 1991. The gastrointestinal absorption of the actinide elements. Science of the Total Environment 100: 43-60.
Fate	Harrison, J.D. and J.W. Stather. 1981. The gastrointestinal absorption of protactinium, uranium and neptunium in the hamster. Radiat Res 88:47-55.
Rev	Hartmann, H. M., F. A. Monette and H. I. Avci. 2000. Overview of Toxicity Data and Risk Assessment Methods for Evaluating the Chemical Effects fo Depleted Uranium Compounds. Human and Ecological Risk Assessment 6(5):851-874.
Not Prim, FL	henRusong (1994). "Summary of the mechanism of U-induced renal damage and its biochemical studies." Govt Reports Announcements & Index(02): 14.
Rev	Hindin, R., D. Brugge, et al. (2005). "Teratogenicity of depleted uranium aerosols: A review from an epidemiological perspective." 4(1): 17.
Acu	Hirsch, G. H. (1972). "Stimulation of renal organic base transport by uranyl nitrate." Can J Physiol Pharmacol 50(6): 533-538.
Fate	Hodge, H. C., F. A. Smith, et al. (1952). "THE EFFECT OF URANIUM-PRODUCED NEPHROSIS IN THE RABBIT ON THE URINARY EXCRETION OF SODIUM FLUORIDE ADMINISTERED IN THE DRINKING WATER." Journal of Pharmacology and Experimental Therapeutics 106(4): 395-395.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Unrel	Holman, R. L. and G. L. Donnelly (1942). "HYPOPROTEINEMIA AS PROTECTION AGAINST MERCURIC CHLORIDE INJURY IN DOGS." J Exp Med 76(6): 511-518.
Unrel; Mix	Houpert, P., F. Paquet, et al. (2001). "Effect of external irradiation on the gastrointestinal absorption of uranium and neptunium in rats." Int J Radiat Biol 77(3): 383-388.
Bio Acc	Houpert, P., S. Frelon, et al. (2007). "Heterogeneous accumulation of uranium in the brain of rats." Radiation Protection Dosimetry 127(1-4): 86-89.
No Oral	Houpert, P., V. Chazel, et al. (1999). "The effects of the initial lung deposit on uranium biokinetics after administration as UF4 and UO4." Int J Radiat Biol 75(3): 373-377.
HHE; Model	Howd, R. A., J. P. Brown, et al. (2000). "Development of California public health goals (PHGs) for chemicals in drinking water." Journal of Applied Toxicology 20(5): 365-380.
No Oral; Gene	Hu, Q. and S. Zhu (1990). "Detection of DNA Damage in Spermiogenic Stages of Mice Treated with Enriched Uranyl Fluoride by Alkaline Elution." Radiation and Environmental Biophysics 29(3): 161-167.
Acu	Ikuma, K., N. Honda, et al. (1986). "Loss of glomerular responses to vasoconstrictor agents in rabbits recovering from acute renal failure." Kidney Int 30(6): 836-841.
Acu	Inoue, S. (1970). "ENZYMATIC STUDIES ON EXPERIMENTAL RENAL INJURIES." Medical Journal of Kobe University 32(2): 59-72.
No Oral	Jadon, A. and R. Mathur (1983). "Gametogenic count and histopathological effect of thorium nitrate and uranyl nitrate on mice testes." Andrologia 15(1): 40-43.
Rev	Jiang, G. C. T. and M. Aschner. 2006. Neurotoxicity of depleted uranium - Reasons for increased concern. Biological Trace Element Research 110(1): 1-17.
Fate:	Jones, E.S. 1966. Microscopic and autoradiographic studies of distribution of urnaium in the rat kidney. Health Phys 12:1437-1451.
Not Prim	Jortner, B. (2004). "Multifactorial Assessment of Depleted Uranium Neurotoxicity." Govt Reports Announcements & Index(23): 100.
Not Prim	Jortner, B. S. (2003). "Multifactorial Assessment of Depleted Uranium Neurotoxicity." Govt Reports Announcements & Index(10): 75.
Not Prim	Jortner, B. S. and D. S. Barber (2002). "Multifactorial Assessment of Depleted Uranium Neurotoxicity." Govt Reports Announcements & Index(24): 26.
Acu	Kathren, R. L. and R. K. Burklin (2008). "Acute chemical toxicity of uranium." Health Physics 94(2): 170-179.
Acu	Kato, A. A. Hishida and T. Nakajima. 1994. Effects of oxygen free radical scavengers on uranium induced acute renal failure in rats. Free Radical Biol Med 16(6):855-859.
FL	Keller, H. 1953. [Blood cholesterine, albuminuria and histological changes in chronic uranium nitrate poisoning in rabbit; contribution to the problem of experimental kidney diseases]. Helv Med Acta 20(3): 157-205.
Fate; Acu	Kennedy, A. and P. G. Saluga (1970). "URINARY CYTOLOGY IN EXPERIMENTAL TOXIC RENAL INJURY." Annals of the Rheumatic Diseases 29(5): 546-552.
Acu	Kleinman, J. G., J. S. McNeil, et al. (1975). "Uranyl nitrate acute renal failure in the dog: early changes in renal function and haemodynamics." Clin Sci Mol Med 48(1): 9-16.
No Oral; Acu	Kobayashi, S., M. Nagase, et al. (1984). "GLOMERULAR ALTERATIONS IN URANYL ACETATE-INDUCED ACUTE RENAL FAILURE IN RABBITS." Kidney International 26(6): 808-815.
No Oral	Kosma, V. M., S. Lang, et al. (1991). "HISTOPATHOLOGICAL EFFECTS OF HOT PARTICLES ON THE SKIN OF MICE." Pathology Research and Practice 187(6): 709.
Surv; Unrel	Kudiasheva, A. G. (2009). "[The dynamics of tundra vole populations and accumulation of natural radionuclides in the territories with increased level of radioactive pollution]." Radiats Biol Radioecol 49(2): 172-178.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Surv	Kudiasheva, A. G., L. N. Shishkina, et al. (2004). "[Monitoring of tundra vole (Microtus oeconomus Pall.) population inhabiting areas with increased radiation background]." Radiats Biol Radioecol 44(3): 262-268.
No Oral	Kupsh, C. C., R. J. Julian, et al. (1991). "Renal damage induced by uranyl nitrate and estradiol-17beta in Japanese quail and Wistar rats." Avian Pathology 20(1): 25-34.
No Control	Kurlyandskaya, E. B. 1970. The Effect Of U3O8 On The Body Of The Pregnant Female And The Foetus. Toxicology of Radioactive Substances. A. A. Letavet and E. B. Kurlyandskaya. Elmsford, NY, Pergamon Press. Vol. 4, Thorium-232 and Uranium-238: 109-119.
HHE	Kurttio, P., A. Auvinen, et al. (2002). "Renal effects of uranium in drinking water." Environmental Health Perspectives 110(4): 337-342.
Unrel	Kuzin, A. M., L. V. Slozhenikina, et al. (1983). "[Possible effect of natural background radiation on the development of mammals]." Radiobiologiia 23(2): 192-195.
In vit	L'Azou, B., M. H. Henge-Napoli, et al. 2002. Effects of cadmium and uranium on some in vitro renal targets. Cell Biology and Toxicology 18(5): 329-340.
Fate; Bio acc	La Touche, Y. D., D. L. Willis and O.I. Dawydiak. 1987. Absorption and biokenetics of U in rats following an oral administration of uranyl nitrate solution. Health Physics 53: 147-162.
HHE; Model	Lam, R. H., J. P. Brown, et al. (1994). Chemicals in california drinking water source of contamination risk assessment and drinking water standards. Wang, R. G. M. (Ed.). Environmental Science and Pollution Control Series, 9. Water Contamination and Health: Integration of Exposure Assessment, Toxicology, and Risk Assessment. Xiv+524p. Marcel Dekker, Inc.: New York, New York, USA; Basel, Switzerland. Isbn 0-8247-8922-9.; 0 (0). 1994. 15-44.
No Oral	Lang, S. and T. Raunemaa (1991). "Behavior of Neutron-Activated Uranium Dioxide Dust Particles in the Gastrointestinal Tract of the Rat." Radiation Research 126(3): 273-279.
Rev	Leggett, R. W. 1989. The behavior and chemical toxicity of U in the kidney: a reassessment. Health Phys 57(3): 365-383.
HHE; Model	Leggett, R. W. (1994). "BASIS FOR THE ICRPS AGE-SPECIFIC BIOKINETIC MODEL FOR URANIUM." Health Physics 67(6): 589-610.
HHE; Rev	Leggett, R. W. and J. D. Harrison (1995). "FRACTIONAL ABSORPTION OF INGESTED URANIUM IN HUMANS." Health Physics 68(4): 484-498.
Unrel	Leonard, A., M. Delpoux, et al. (1979). "NATURAL RADIOACTIVITY IN SOUTHWEST FRANCE AND ITS POSSIBLE GENETIC CONSEQUENCES FOR MAMMALS." Radiation Research 77(1): 170-181.
No Oral; Acu	Liapis, H., G. Vogler, et al. 1997. North American opossum Didelphis virginiana as a fetal nephrotoxicity model: histologic and ultrastructural assessment of uranyl nitrate (UN)-induced damage. Microsc Res Tech 39(3): 285-296.
Acu	Lim, I. K., K. H. Lee, et al. (1987). "Uranyl nitrate induced polyuric acute tubular necrosis in rats." Yonsei Med J 28(1): 38-48.
In vit	Lin, R. H., L. J. Wu, et al. (1993). "Cytogenetic toxicity of uranyl nitrate in Chinese hamster ovary cells." Mutation Research 319(3): 197-203.
Abstract	Linsalata, P. (1987). "The morro do ferro brazil natural analogue an update of findings related to the mobilization and biological incorporation of transuranic analogue elements." Thirty-Second Annual Meeting of the Health Physics Society, Salt Lake City, Utah, USA, July 5-9, 1987. Health Phys 52(SUPPL. 1): S55.
Surv; Fate	Linsalata, P., R. Morse, et al. (1989). "Transport pathways of thorium, uranium, radium and lanthanum from soil to cattle tissues." Journal of Environmental Radioactivity 10(2): 115-140.
Fate; No Oral	Lloyd, R. D., E. Polig, et al. (1996). "Uranium skeletal dosimetry and distribution in young adult beagles: A guide for calculating uranium skeletal doses in humans." Health Physics 70(3): 396-401.
No Oral	Lopez, R., P. L. D. Sylvester, et al. (2000). "Percutaneous toxicity of uranyl nitrate: Its effect in terms of exposure area and time." Health Physics 78(4): 434-437.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Surv; Unrel	Lottermoser, B. G., H. J. Glass, et al. (2011). "Sustainable natural remediation of abandoned tailings by metal-excluding heather (Calluna vulgaris) and gorse (Ulex europaeus), Carnon Valley, Cornwall, UK." Ecological Engineering 37(8): 1249-1253.
Rev	Macnider, W. D. (1917). "A CONSIDERATION OF THE RELATIVE TOXICITY OF URANIUM NITRATE FOR ANIMALS OF DIFFERENT AGES. I." J Exp Med 26(1): 1-17.
Acu; No Oral	Macnider, W. D. (1919). "A FUNCTIONAL AND PATHOLOGICAL STUDY OF THE CHRONIC NEPHROPATHY INDUCED IN THE DOG BY URANIUM NITRATE." J Exp Med 29(5): 513-529.
Acu; No Oral	Macnider, W. D. (1929). "The development of the chronic nephritis induced in the dog by uranium nitrate. A functional and pathological study with observations on the formation of urine by the altered kidneys." Journal of Experimental Medicine 49(3): 387-410.
No Oral	Mahmood, I. and D. H. Waters (1994). "A comparative study of uranyl nitrate and cisplatin-induced renal failure in rat." Eur J Drug Metab Pharmacokinet 19(4): 327-336.
Acu; No Oral	Malard, V., J. C. Gaillard, et al. (2009). "Urine proteomic profiling of uranium nephrotoxicity." Biochimica Et Biophysica Acta-Proteins and Proteomics 1794(6): 882-891.
FL	Malenchenko, A. F. (1970). "EFFECT OF URANIUM ON THE FUNCTION AND DISTRIBUTION OF IODINE IN THE THYROID." Doklady Akademii Nauk Belorusskii SSR 14(4): 376-378.
No Oral; FL	Malenchenko, A. F., V. I. Bakhanovich, et al. 1971. Effect of uranium nitrate on the morpho functional state of rabbit thyroid gland. Byulleten' Eksperimental'noi Biologii i Meditsiny 71(3): 36-38.
Acu; FL	Malyenchanka, A. F. and H. V. Kazyuk (1972). "EFFECT OF URANYL NITRATE ON THE FUNCTION OF THE RAT THYROID." Vyestsi Akademii Navuk BSSR Syeryya Biyalahichnykh Navuk(6): 71-75.
IMM	Malyenchanka, A. F. and N. A. Barkun (1976). "EFFECT OF URANIUM INTOXICATION ON THE COURSE OF AUTO IMMUNE ALLERGIC ORCHITIS IN RATS." Vyestsi Akademii Navuk BSSR Syeryya Biyalahichnykh Navuk 2: 96-101.
Acu; Mix	Martinez, A. B., R. L. Cabrini, et al. (2000). "Orally administered ethane-1-hydroxy-1,1-biphosphonate reduces the lethal effect of oral uranium poisoning." Health Physics 78(6): 668-671.
Abstract	Marumo, F., H. Takami, et al. (1992). "Endothelin et-1 production in the rabbit nephron of uranium-induced acute renal failure arf." 25th Annual Meeting of the American Society of Nephrology, Baltimore, Maryland, USA, November 15-18, 1992. J Am Soc Nephrol 3(3): 441.
Surv; Unrel	Materii, L. D. and K. I. Maslova (1978). "MICRO NUCLEI IN PERIPHERAL BLOOD CELLS OF MICROTUS-OECONOMUS LIVING IN AREAS OF ENHANCED NATURAL RADIOACTIVITY." Radiobiologiya 18(6): 919-922.
Surv	Materii, L. D. and K. I. Maslova (1984). "[Effect of increased natural radioactivity on bone marrow morphology of Microtus oeconomus pall]." Radiobiologiia 24(2): 243-246.
Acu; No Oral	Mauk, R. H., R. V. Patak, et al. (1977). "EFFECT OF PROSTAGLANDIN E ADMINISTRATION IN A NEPHRO TOXIC AND A VASO CONSTRICTOR MODEL OF ACUTE RENAL FAILURE." Kidney International 12(2): 122-130.
Dup	Maynard, E. A., C. Randall, et al. 1949. Effects of feeding uranium nitrate hexahydrate in the diets of breeding white rats. Journal of Pharmacology and Experimental Therapeutics 95(4): 421-428.
Abstract	Maynard, E. A., C. Randall, et al. (1947). "Effects of feeding uranium nitrate in the diets of breeding white rats." Federation Proceedings 6(1): 355.
No Oral	McClain, D.E., Benson, K.A., Dalton, T.K., 2001. Biological effects of embedded depleted uranium (DU): summary of Armed Forces Radiobiology Research Institute research. Sci. Total Environ. 274, 115–118.
Dup	McDonald-Taylor, C. K., A. Singh, et al. 1997. Uranyl nitrate-induced proximal tubule alterations in rabbits: A quantitative analysis. Toxicologic Pathology 25(4): 381-389.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Mix	Mikhailov, M. A., D. Kr"Stanov, et al. (1986). "ON THE CHANGES IN THE ACTIVITY OF SOME ENZYMES IN THE COMBINED URANIUM INJURIES." Problemi na Rentgenologiyata i Radiobiologiyata 7: 152-155.
Rev	Miller, A. C. and D. McClain. 2007. A review of depleted uranium biological effects: in vitro and in vivo studies. Rev Environ Health 22(1): 75-89.
No Oral; Gene	Miller, A. C., Stewart, M., Brooks, K., Shi, L., Page, N. 2002. Depleted uranium-catalyzed oxidative DNA damage: absence of significant alpha particle decay. Journal of Inorganic Biochemistry 91: 246-252.
No Oral; Gene; Imm	Monleau, M., DeMeo, M., Paquet, F., Chazel, V., Dumenil, G., Donnadieu-Claraz, M. 2006. Genotoxic and Inflammatory Effects of Depleted Uranium Particles Inhales by Rats. Toxicological Sciences. 89(1): 287-295.
Unrel	Moreira-Nordemann, L. M. and G. Sieffermann (1979). "DISTRIBUTION OF URANIUM IN SOIL PROFILES OF BAHIA STATE BRAZIL." Soil Science 127(5): 275-280.
HHE; Model	Morris, S. C. and A. F. Meinhold (1995). "PROBABILISTIC RISK ASSESSMENT OF NEPHROTOXIC EFFECT OF URANIUM IN DRINKING-WATER." Health Physics 69(6): 897-908.
Mix	Moxon, A. L. and K. P. DuBois (1939). "The Influence Of Arsenic And Certain Other Elements On The Toxicity Of Seleniferous Grains." Journal of Nutrition 18(5): 447-457.
Abstract	Munson, J. W., J. K. Tolson, et al. (2003). "Heat shock proteins and uranium nephrotoxicity." Toxicological Sciences 72(S-1): 347.
Unrel	Narayana, K. and M. Al-Bader (2011). "Ultrastructural and DNA damaging effects of lead nitrate in the liver." Exp Toxicol Pathol 63(1-2): 43-51.
Unrel	Nayman, J. (1964). "INDUCTION OF REVERSIBLE AND IRREVERSIBLE PATTERNS OF RENAL FAILURE. A REPRODUCIBLE LABORATORY PREPARATION IN THE DOG." J Surg Res 4: 82-91.
Rev	Nolte, T., J. H. Harleman, et al. (1995). "Histopathology of chemically induced testicular atrophy in rats." Experimental and Toxicologic Pathology 47(4): 267-286.
No Oral	Nomiyama, K. and E. C. Foulkes. 1968. Some effects of uranyl acetate on proximal tubular function in rate kidney. Toxicol. Appl. Pharmacol. 13: 89-98.
Meth; Acu	Nomiyama, K., A. Yamamoto, et al. (1974). "Assay of urinary enzymes in toxic nephropathy." Toxicol Appl Pharmacol 27(3): 484-490.
FL	Novikov, I. V. (1972). "[Hygienic standardization of the permissible level of uranium in drinking water]." Gig Sanit 37(9): 13-17.
FL	Novikov, I. V. and T. V. Iudina (1970). "[Effect of uranium on the phosphatase activity]." Farmakol Toksikol 33(2): 230-231.
Rev	Novikov, I. V. and T. V. Iudina. 1970. Effect of uranium on the phosphatase activity. Farmakol Toksikol 33(2): 230-231.
Rev; Unrel	Novikov, Y. V. (1970). "Regarding hygienic standards for natural uranium content of water." Gig Sanit 35(5): 83-88.
Model; Fate	O'Flaherty, E. J. (1995). "PBK Modeling for Metals. Examples with Lead, Uranium, and Chromium." Toxicol Lett 82(83): 367-372.
Nut	Opie, E. L. and L. B. Alford (1915). "THE INFLUENCE OF DIET UPON NECROSIS CAUSED BY HEPATIC AND RENAL POISONS : PART II. DIET AND THE NEPHRITIS CAUSED BY POTASSIUM CHROMATE, URANIUM NITRATE, OR CHLOROFORM." J Exp Med 21(1): 21-37.
Surv	Owen, D. E. and J. K. Otton (1995). "MOUNTAIN WETLANDS - EFFICIENT URANIUM FILTERS - POTENTIAL IMPACTS." Ecological Engineering 5(1): 77-93.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Surv; Fate	Paquet, F., E. Ansoborlo, et al. (1998). "Biological speciation in the field of internal dosimetry." Journal De Chimie Physique Et De Physico-Chimie Biologique 95(4): 845-850.
In vit	Park, J. H. and H. S. Kwun (1973). "INFLUENCE OF NEPHRO TOXIC AGENTS ON JUXTAGLOMERULAR CELLS OF MICE." Journal of Catholic Medical College 24: 31-43.
Acu	Pavlakis, N., C. A. Pollock, et al. (1996). "Deliberate overdose of uranium: Toxicity and treatment." Nephron 72(2): 313-317.
Acu	Pelayo, J. C., P. M. Andres, et al. (1983). "THE INFLUENCE OF AGE ON ACUTE RENAL TOXICITY OF URANYL NITRATE IN THE DOG." Pediatric Research 17(12): 985-992.
Abstract	Pelayo, J. C., P. M. Andrews, et al. 1981. The influence of age on uranyl nitrate nephro toxicity. Pediatric Research 15(4 PART 2): 675.
Abstract	Pelayo, J. C., P. M. Andrews, et al. 1981. The influence of age on uranyl nitrate nephro toxicity. Kidney International 19(1): 211.
No Oral	Pellmar, T. C., J. B. Hogan, et al. (1998). "Toxicological Evaluation of Depleted Uranium in Rats: Six-Month Evaluation Point." Govt Reports Announcements & Index(14): 28.
In vit	Petitot, F., A. M. Moreels, et al. (2004). "In vitro evaluation of percutaneous diffusion of uranyl nitrate through intact or excoriated skin of rat and pig." Can J Physiol Pharmacol 82(2): 133-139.
No Oral	Petitot, F., A. M. Moreels, et al. (2010). "Evolution of the percutaneous penetration and distribution of uranyl nitrate as a function of skin-barrier integrity: an in vitro assessment." Drug and Chemical Toxicology 33(3): 316-324.
No Oral	Petitot, F., C. Gautier, et al. (2007). "Percutaneous penetration of uranium in rats after a contamination on intact or wounded skin." Radiat Prot Dosimetry 127(1-4): 125-130.
Surv; Fate	Popovic, D., T. Bozic, et al. (2010). "Concentration of trace elements in blood and feed of homebred animals in Southern Serbia." Environmental Science and Pollution Research International 17(5): 1119-1128.
FL	Porte, A., Y. Cussac, et al. (1963). "[ON THE FORMATION AND ULTRASTRUCTURE OF "REGENERATION CELLS" IN THE RENAL TUBULES OF MICE POISONED BY URANYL NITRATE]." C R Seances Soc Biol Fil 157: 2079-2081.
Rev	Priest, N.D. 2001. Toxicity of depleted uranium. Lancet 357: 244-46.
Surv; Unrel	Prikryl, J. D., D. A. Pickett, et al. (1997). "Migration behavior of naturally occurring radionuclides at the Nopal I uranium deposit, Chihuahua, Mexico." Journal of Contaminant Hydrology 26(1-4): 61-69.
Abstract	Prokes, J., S. Sromova, et al. (1991). "Hormetic effect of low doses of uranium in rats." Science of the Total Environment 101(1-2): 161.
In vit	Prokes, J., T. Haas, et al. (1994). "Hormesis in effect of low uranium doses on organisms." Sb Lek 95(4): 347-355.
Acu; No Oral	Pujadas Bigi, M. M. and A. M. Ubios (2007). "Catch-up of delayed tooth eruption associated with uranium intoxication." Health Physics 92(4): 345-348.
Acu	Pujadas Bigi, M. M., L. Lemlich, et al. (2003). "Exposure to oral uranyl nitrate delays tooth eruption and development." Health Physics 84(2): 163-169.
HHE; Model	Rayno, D. R. (1983). "ESTIMATED DOSE TO MAN FROM URANIUM MILLING VIA THE BEEF MILK FOOD CHAIN PATHWAY." Science of the Total Environment 31(3): 219-242.
Rev	Ribera, D. F. Labrot, G. Tisnerat and J. Narbonne. 1996. Uranium in the Environment: Occurrence, Transfer, and Biological Effects. Reviews of Environmental Contamination and Toxicology 146:53-89.
No Oral	Rodriquez-Yoldi, M. J. and F. Ponz. 1986. Uranyl action on sugar transport across rat jejunum. Rev. Esp. Fisiol. 42:359-364.
No Oral	Rossi, J. d., M. Y. Bekkedal, et al. (2004). "Failure To Detect Differences In The Neurobehavioral Development Of Rats Following In Utero And Pre-Weanling Exposure To Depleted Uranium." Neurotoxicology 25(4): 718-719.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Dup	Sanchez, D. J., M. Belles, et al. 2006b. Combined action of uranium and restraint stress in pregnant rats: developmental and behavioral effects in the offspring. Metal Ions in Biology and Medicine, Vol 9. M. C. Alpoim and P. V. Morais. Montrouge, John Libbey Eurotext. 9: 431-434.
Unrel	Schmidt, P. and T. Lindner (2006). Development of water-borne radioactive discharges at WISMUT and resulting radiation exposures, Springer-Verlag Berlin, Heidelberger Platz 3, D-14197 Berlin, Germany.
Fate	Seidel, A., U. Sutterlin, et al. (1982). "SPECIES DIFFERENCES IN THE RETENTION OF TRANS URANIUM ELEMENTS AND TRITON WR-1339 IN RAT AND CHINESE HAMSTER LIVER LYSOSOMES." Biology of the Cell (Paris) 45(2): 220.
Diss, Carcin; Invit	Servomaa, K. (1991). "Biological effects of radiation: The induction of malignant transformation and programmed cell death." Govt Reports Announcements & Index(10): 132.
Unrel	Sharma, S. N., V. P. Kamboj, et al. (1972). "CALCIFICATION OF THE RAT TESTIS BY SOME RARE EARTH AND RADIOACTIVE METALLIC SALTS." Experimentelle Pathologie (Jena) 7(3-4): 176-181.
Surv; Rev	Sheppard, M.I., 1980. The environmental behavior of uranium and thorium. Whiteshell Nuclear Research Establishment, Atomic Energy of Canada Limited, Pinawa, Manitoba, 44 pp. (Technical Report AECL-6795).
HHE; Model	Sheppard, S. C. (1998). "Geophagy: Who eats soil and where do possible contaminants go?" Environmental Geology (Berlin) 33(2-3): 109-114.
Rev	Sheppard, S.C., 1989. Toxicity Levels of Arsenic and Uranium in Soils. Atomic Energy of Canada Limited. Technical Record TR-480.
Rev	Sheppard, S.C., 2003. Literature Survey Regarding the Radiotoxicity and the Chemical Toxicity of Uranium on Organisms Other than Humans. Rapport Andra SURRP0ECM03001C, Andra, Chaˆ tenay Malabry Ce´ dex, France.
Bio acc	Sheppard, S.C., Evenden, W.G., 1992. Bioavailability indices for uranium: effect of concentration in eleven soils. Archives of Environmental Contamination and Toxicology 23, 117–124.
Meth	Sheppard, S.C., Evenden, W.G., Anderson, A.J., 1992. Multiple assays of uranium toxicity in soil. Environmental Toxicology and Water Quality: An International Journal 7, 275–294.
Rev	Sheppard, S.C., Sheppard, M.I., Gallerand, M., Sanipelli, B., 2005. Derivation of ecotoxicity thresholds for uranium. Journal of Environmental Radioactivity 79, 55–83.
Invert	Sheppard, S.C., Sheppard, M.I., Sanipelli, B., Dowsley, B., Stephenson, G., Feisthauer, N., Rowland, R., Gilbertson, M.-K., 2004. Uranium Concentrations in Port Hope Soils and Vegetation and Toxicological Effect on Soil Organisms. Canadian Nuclear Safety Commission contract report 87055-01-0266-R161.1, February 2004.
Abstract	Sikov, M. R. and B. J. Kelman (1989). "Factors affecting the placental transfer of actinides." 26th Hanford Life Sciences Symposium on Modeling for Scaling to Man: Biology, Dosimetry, and Response. Health Phys 57(SUPPL. 1): 109-114.
Abstract	Sikov, M. R. and D. N. Rommereim (1986). "Evaluation of the embryotoxicity of uranium in rats." Teratology 33(3): 41C.
Abstract	Singh, A., A. P. Gilman, et al. (1985). "Rabbit renal morphology induced by 91 days exposure to uranyl nitrate 3. a 45-day recovery study." American Association of Anatomists 98th Annual Meeting and the Association Canadienne Des Anatomistes (Canadian Association of Anatomists) 29th Annual Meeting, Toronto, Ont., Canada, May 5-9, 1985. Anat Rec 211(3): 178A.
Abstract	Singh, A., V. E. Gilman, et al. (1985). "Rabbit renal morphology induced by uranyl nitrate 2. high dose 91-day exposure." Meeting of the American Association of Veterinary Anatomists, Baton Rouge, La., USA, July, 1984. Anat Histol Embryol 14(1): 91-92.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Abstract	Singh, N. P. and M. E. Wrenn (1988). "Determinations of actinides in biological and environmental samples." Fifth Symposium on Environmental Radiochemical Analysis, Part B, Harwell, England, Uk, October 1-3, 1986. Sci Total Environ 70(0): 187-204.
Fate	Singh, N. P. and M. E. Wrenn (1989). "Is the Beagle Dog an Appropriate Experimental Animal for Extrapolating Data to Humans on Organ Distribution Patterns of U, Th, and Pu?" Health Physics 57(1): 91-96.
No Oral	Singhvi, S. M., A. F. Heald, et al. (1978). "DISPOSITION OF CARBON-14 NADOLOL IN DOGS WITH REVERSIBLE RENAL IMPAIRMENT INDUCED BY URANYL NITRATE." Toxicology and Applied Pharmacology 43(1): 99-110.
Unrel	Slozhenikina, L. V., L. A. Fialkovskaia, et al. (1985). "[Possible effect of natural radioactivity on the induction of glucokinase synthesis in the liver of developing rats]." Radiobiologiia 25(2): 227-230.
FL	Souidi, M., E. Tissandie, et al. 2009. Uranium: properties and biological effects after internal contamination. Annales De Biologie Clinique 67(1): 23-38.
In vit	Spruit, D. and J. P. Kuiper (1967). "The Interaction of Some Metal Ions with the Uterus of the Guinea Pig." Acta Physiologica et Pharmalogica Neerlandica 14(4): 434-442.
Acu	Stein, J. H., J. Gottschall, et al. (1975). "Pathophysiology of a nephrotoxic model of acute renal failure." Kidney International 8(1): 27-41.
No Oral	Steinhardt, G., L. Salinasmadrigal, et al. (1992). "Fetal nephrotoxicity." Journal of Urology 148(2): 760-763.
No Oral	Still, K. R. and D. P. Arfsten (2005). "Characterization of the Reproductive Toxicity of Depleted Uranium." Govt Reports Announcements & Index(06): 155.
No Oral; Acu	Stone, R. S., S. A. Bencosme, et al. (1961). "Renal Tubular Fine Structure." Archives of Pathology 71: 160-174.
Unrel	Storer, J. B. and R. L. Ullrich (1983). "Life shortening in BALB/c mice following brief, protracted, or fractionated exposures to neutrons." Radiat Res 96(2): 335-347.
No Oral	Stradling, G. N., J. W. Stather, et al. (1989). "THE METABOLIC BEHAVIOR OF URANIUM OCTOXIDE BEARING RESIDUES AFTER THEIR DEPOSITION IN THE RAT LUNG - THE IMPLICATIONS FOR OCCUPATIONAL EXPOSURE." Experimental Pathology 37(1-4): 76-82.
Unrel	Stroo, W. E. and J. B. Hook (1977). "Enzymes of renal origin in urine as indicators of nephrotoxicity." Toxicol Appl Pharmacol 39(3): 423-434.
No Oral	Stuart, B. O., D. H. Willard, et al. (1970). "Studies of inhaled radon daughters, uranium ore dust, diesel exhaust, and cigarette smoke in dogs and hamsters." Inhaled Part 1: 543-560.
Fate; Mix	Sullivan, M. F. and P. S. Ruemmler (1988). "Absorption of 233U, 237Np, 238Pu, 241Am and 244Cm from the gastrointestinal tracts of rats fed an iron-deficient diet." Health Phys 54(3): 311-316.
Fate	Sullivan, M. F., P. S. Ruemmler, et al. (1986). "Influence of oxidizing or reducing agents on gastrointestinal absorption of U, Pu, Am, Cm and Pm by rats." Health Physics 50(2): 223-232.
Fate	Sullivan, M.F. 1980. Absorption of actinides elements from the gastro-intestinal tract of neonatal animals. Health Phys 38:173-185.
No Oral	Sun, Y., Y. Fujigaki, et al. 2011. Acquired resistance to rechallenge injury in rats that recovered from mild renal damage induced by uranyl acetate: accelerated proliferation and hepatocyte growth factor/c-Met axis. Clinical and Experimental Nephrology 15(5): 666-675.
Mix	Svyatkina, N. S. and V. Novikov Yu (1974). "EXPERIMENTAL STUDY OF THE COMBINED EFFECT OF URANIUM AND RADIUM ON THE BODY." Gigiena i Sanitariya(8): 35-41.
Abstract	Swanson, S. M. and N. Roest (1997). "Biophysical effects of uranium mining in canada and some suggestions for biomarkers of effects." Twenty-Third Annual Aquatic Toxicity Workshop, Calgary, Alberta, Canada, October 7-9, 1996. Canadian Technical Report of Fisheries and Aquatic Sciences 0(2144): 33.

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Rev	Sztajnkrycer, M. D. and E. J. Otten. 2004. Chemical and radiological toxicity of depleted uranium. Military Medicine 169(3): 212-216.
Bio acc	Tannenbaum A, Silverstone H, Koziol J. 1951. Tracer studies of the distribution and excretion of uranium in mice, rats, and dogs. In: Tannenbaum A, ed. Toxicology of uranium compounds. New York, NY: McGraw-Hill, 128-181.
No Oral	Tannenbaum, A. and H. Silverstone (1946). "Relationship Of Uranium Excretion To The Total Amount Of Uranium In The Mouse." Michael Reese Hospital, Chicago, Illinois, Report No. CH 3616.
Acu	Tao, Z. Q., X. H. Xu, et al. (1987). "DETOXICATION AND MOBILIZATION OF URANIUM BY CATECHOLAMIC ACID." Acta Pharmacologica Sinica 8(3): 284-288.
Acu	Taulan, M., F. Paquet, et al. (2006). "Comprehensive analysis of the renal transcriptional response to acute uranyl nitrate exposure." Bmc Genomics 7: article #2.
Rev	Taylor DM, Taylor SK. 1997. Environmental uranium and human health. Rev Environ Health 12:147–57.
Bio acc	Tessier, C., D. Suhard, et al. 2012. Uranium Microdistribution in Renal Cortex of Rats after Chronic Exposure: A Study by Secondary Ion Mass Spectrometry Microscopy. Microscopy and Microanalysis 18(1): 123-133.
In vit; Gene	Thiebault, C., M. Carriere, et al. 2007. Uranium induces apoptosis and is genotoxic to normal rat kidney (NRK-52E) proximal cells. Toxicol Sci 98(2): 479-487.
Surv	Thomas, P. A. (2000). "Radionuclides in the terrestrial ecosystem near a Canadian uranium mill - Part II: Small mammal food chains and bioavailability." Health Physics 78(6): 625-632.
Surv	Thomas, P. A. and T. E. Gates (1999). "Radionuclides in the lichen-caribou-human food chain near uranium mining operations in northern Saskatchewan, Canada." Environmental Health Perspectives 107(7): 527-537.
Surv	Thomas, P., J. lrvine, et al. (2005). "Radionuclides and trace metals in Canadian moose near uranium mines: Comparison of radiation doses and food chain transfer with cattle and caribou." Health Physics 88(5): 423-438.
In vit	Thompson, J. D. and B. R. Nechay. 1981. Inhibition by metals of a canine renal calcium magnesium atpase. Journal of Toxicology and Environmental Health 7(6): 901-908.
Model	Thompson, P. A., J. Kurias, et al. 2005. Derivation and use of sediment quality guidelines for ecological risk assessment of metals and radionuclides released to the environment from uranium mining and milling activities in Canada. Environmental Monitoring and Assessment 110(1-3): 71-85.
Bio acc	Thorne, M. C. 2003. Estimation of animal transfer factors for radioactive isotopes of iodine, technetium, selenium and uranium. Journal of Environmental Radioactivity 70:3-20.
Acu	Tissandie E, Gueguen Y, Lobaccaro JM, et al. 2006. Effects of depleted uranium after short-term exposure on vitamin D metabolism in rat. Arch Toxicol 80(8):473-480.
Acu	Tissandie, E., Y. Gueguen, et al. (2005). Effects of short term depleted uranium exposure on vitamin D-3 cytochromes P450 metabolizing enzymes in rat. 40128 Bologna, Medimond S R L.
Dup	Tissandie, E., Y. Gueguen, et al. (2008). "Enriched uranium affects the expression of vitamin D receptor and retinoid X receptor in rat kidney." Journal of Steroid Biochemistry and Molecular Biology 110(3-5): 263-268.
No Control	Tolgskaya, M. S. 1970. Pathomorphological Changes In Animals Following Acute And Chronic Poisoning With U3O8. Toxicology of Radioactive Substances 4(232): 120-135.
Bio acc	Tomilin, Y. A., N. V. Vintsukevich, et al. (1987). "Preliminary radiation-hygienic evaluation of the meat of animals whose food was supplemented with mine water." Vopr Pitan 0(1): 61-64.
Fate	Tracy, B. L., J. M. Quinn, et al. (1992). "Absorption and retention of uranium from drinking water by rats and rabbits." Health Phys 62(1): 65-73.
Acu; No Oral	Tyrakowski, T. (1979). "Disturbances in electrolyte transport in uranyl ion intoxication: Model studies on the preliminary stage of toxic acute renal failure: 2. The effect of uranyl acetate on the kidney in vivo." Acta Med Pol 20(4): 1980).

Table A-3. Papers rejected for use in the development of a mammalian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Acu; No Oral	Tyrakowski, T. (1979). "Disturbances in electrolyte transport in uranyl ion intoxication: Model studies on the preliminary stage of toxic acute renal failure: 3. Disturbances in sodium and potassium ion excretion and decrease in glomerular filtration rate following uranyl acetate intoxication." Acta Medica Polona 20(4): 317-330.
Acu; No Oral; Mix	Ubios, A. M. (1994). "Mechanisms of uranium intoxication in bone - An approach to the study of detoxification methods. Final report for the period December 1989 - December 1993." Govt Reports Announcements & Index(01): 11.
No Oral	Ubios, A. M., M. B. Guglielmotti, et al. (1991). "Uranium inhibits bone formation in physiologic alveolar bone modeling and remodeling." Environ Res 54(1): 17-23.
No Oral	Ubios, A. M., M. Marzorati, et al. (1997). "Skin alterations induced by long-term exposure to uranium and their effect on permeability." Health Physics 72(5): 713-715.
Model	Uijt de Haag, P. A. M., R. C. G. M. Smetsers, et al. 2000. Evaluating the risk from depleted uranium after the Boeing 747-258F crash in Amsterdam, 1992. Journal of Hazardous Materials 76(1): 39-58.
Abstract	Ungvary, G., E. Szakmary, et al. (2000). "On the embryotoxic and teratogenic effects of 'low-radiation' uranium." Journal of Physiology (Cambridge) 526P: 186P.
Bio acc; Surv	Van Netten, C. and D. R. Morley (1982). "UPTAKE OF URANIUM AND MOLYBDENUM FROM URANIUM RICH SOILS BY BARLEY." International Journal of Environmental Studies 19(1): 43-46.
Unrel	Vasilenko, I. and O. I. Vasilenko. 2006. Chronic radiation damage by uranium and plutonium nuclear fission products. Radiats Biol Radioecol 46(6): 735-740.
Acu; Unrel	Wachstein, M. (1946). "INFLUENCE OF EXPERIMENTAL KIDNEY DAMAGE ON HISTOCHEMICALLY DEMONSTRABLE LIPASE ACTIVITY IN THE RAT. COMPARISON WITH ALKALINE PHOSPHATASE ACTIVITY." J Exp Med 84(1): 25-36.
Fate	Walinder, G. 1989. Metabolism and sites of effects of uranium after incorportation along different routes in mice, rabbits and piglets. Radiat Prot Dosim 26(1/4):89-95.
Model	Wenzel, W. J., A. F. Gallegos, et al. (1982). "DYNAMIC MODELING OF AGRICULTURAL PATHWAYS IN 3 TERRESTRIAL ECOSYSTEMS FOR PLUTONIUM AND URANIUM." Health Physics 43(1): 168.
Not Prim	Wolfe, G. W. and L. W. Condie (1994). Health effect studies on recycled drinking water from secondary wastewater au - lauer wc. Yang, R. S. H. (Ed.). Toxicology of Chemical Mixtures: Case Studies, Mechanisms, and Novel Approaches. Xxiv+720p. Academic Press, Inc.: San Diego, California, USA; London, England, Uk. Isbn 0-12-768350-X.; 0 (0). 1994. 63-81.
Rev; Fate	Wrenn ME, Durbin PW, Howard B, Lipsztein J, Rundo J, Still ET, Willis DL. 1985. Metabolism of ingested U and Ra. Health Phys 48:601–33.
Rev	Wrenn, M.D.E., P. W. Durbin, D. L. Willis and N. P. Singh. 1987. The potential toxicity of uranium in water. Am. Water Works Assoc J 79(4):177-184.
Alt	Zalups, R. K., R. M. Gelein, et al. (1988). "Nephrotoxicity of uranyl fluoride in uninephrectomized and sham-operated rats." Toxicol Appl Pharmacol 94(1): 11-22.
Gene; FL	Zhu, S. P., Q. Y. Hu, et al. (1994). "[Studies on reproductive toxicity induced by enriched uranium]." Zhonghua Yufang Yixue Zazhi 28(4): 219-222.
Acu; No Oral	Zimmerman, K. L., D. S. Barber, et al. 2007. Temporal clinical chemistry and microscopic renal effects following acute uranyl acetate exposure. Toxicologic Pathology 35(7): 1000-1009.

Notes:

Reference citations are presented as obtained from the abstract review and have not been edited, and in some cases abbreviated. Full citations are available upon request.

Table A-4. Papers rejected for use in the development of an avian toxicity reference value for uranium.

Reject Code	Reference
Bio acc	Anke, M., O. Seeber, et al. (2009). "Uranium transfer in the food chain from soil to plants, animals and man." Chemie Der Erde-Geochemistry 69: 75-90.
Bio acc	Bird, G. A. and W. G. Evenden (1996). "Transfer of 60Co, 65Zn, 95Tc, 134Cs and 238U from water to organic sediment." Water Air and Soil Pollution 86(1-4): 251-261.
Bio acc	Burger, J. and M. Gochfeld (2007). "Metals and radionuclides in birds and eggs from Amchitka and Kiska Islands in the Bering Sea/Pacific Ocean ecosystem." Environmental Monitoring and Assessment 127(1-3): 105-117.
Bio acc	Casacuberta, N., P. Masque, et al. (2008). Incorporation of Pb-210 and Po-210 to poultry through the addition of Dicalcium Phosphate (DCP) to the diet. Natural Radiation Environment. A. S. Paschoa and F. Steinhausler. Melville, Amer Inst Physics. 1034: 295-298.
Unrel, Bio acc	Clulow, F. V., T. P. Lim, et al. (1992). "Radium-226 levels and concentration ratios between water, vegetation, and tissues of ruffed grouse (Bonasa umbellus) from a watershed with uranium tailings near Elliot Lake, Canada." Environmental Pollution 77(1): 39-50.
Bio acc	Dowdall, M., S. Gerland, et al. (2003). "Gamma-emitting natural and anthropogenic radionuclides in the terrestrial environment of Kongsfjord, Svalbard." Science of the Total Environment 305(1-3): 229-240.
Rev	Fesenko, S., B. J. Howard, et al. (2009). "Review of Russian-language studies on radionuclide behaviour in agricultural animals: part 4. Transfer to poultry." Journal of Environmental Radioactivity 100(10): 815-822.
Rev	Gagnaire, B., C. Adam-Guillermin, et al. (2011). "The effects of radionuclides on animal behavior." Rev Environ Contam Toxicol 210: 35-58.
Acu; No Oral	Harvey, R.B., Kubena, L.F., Lovering, S.L., Mollenhauer, H.H., Phillips, I.D., (1986a). Acute toxicity of uranyl nitrate to growing chicks: a pathophysiologic study. Bulletin of Environmental Contamination and Toxicology 37, 907–915.
Acu; Alt; No Oral	Harvey, R. B., L. F. Kubena, et al. (1986b). "Validation of Impaired Renal Function Chick Model with Uranyl Nitrate." Bulletin of Environmental Contamination and Toxicology 36(1): 67-72.
Bio acc	Jeambrun, M., L. Pourcelot, et al. (2012). "Study on transfers of uranium, thorium and decay products from grain, water and soil to chicken meat and egg contents." J Environ Monit.
Bio acc	Kapsimalis, R., S. Landsberger, et al. (2009). "The determination of uranium in food samples by Compton suppression epithermal neutron activation analysis." Applied Radiation and Isotopes 67(12): 2097-2099.
Mix	Lin-Shiau, S. Y. (1983). "Selective antagonism by uranyl nitrate against Formosan Krait venom--Part I." Taiwan Yi Xue Hui Za Zhi 82(5): 640-643.
No oral	Moitra, P. K., K. Paul, et al. (1997). "Teratogenic effect of uranyl acetate on developing chick embryos." Indian Journal of Physiology and Allied Sciences 51(2): 65-71.
Surv, No Prim	Osborne, D. R., D. M. Ambrose, et al. (1992). "Characterization of reproduction and growth of American robins at the Fernald Environmental Management Project, 1991." Govt Reports Announcements & Index(16): 49.
FL; Bio acc	ouLanxing, uShiming, et al. (1996). "Investment of radioactivity background in agroenvironment around Daya-Bay NPP." Govt Reports Announcements & Index(01): 10.
Unrel	Ramirez, P. and B. P. Rogers (2002). "Selenium in a Wyoming grassland community receiving wastewater from an in situ uranium mine." Archives of Environmental Contamination and Toxicology 42(4): 431-436.
Bio acc	Robinson, G. A. (1988). "Distribution of nanomole quantities of uranium-235 in young and adult japanese quail and in the f-1 generation comparison with gadolinium-153." Nuclear Medicine and Biology 15(3): 277-284.

Table A-4. Papers rejected for use in the development of an avian toxicity reference value for uranium. (Continued)

Reject Code	Reference
Bio acc	Robinson, G. A., C. C. Kupsh, et al. (1986). "Increased deposition of uranium in the bones of vitellogenic male japanese quail effect of estradiol-17-beta on the distribution of uranium-vi thorium-iv gadolinium-iii and calcium-ii." Poult Sci 65(6): 1178-1183.
Bio acc	Robinson, G. A., D. C. Wasnidge, et al. (1984). "A COMPARISON OF THE DISTRIBUTIONS OF THE ACTINIDES URANIUM AND THORIUM WITH THE LANTHANIDE GADOLINIUM IN THE TISSUES AND EGGS OF JAPANESE QUAIL CONCENTRATIONS OF URANIUM IN FEEDS AND FOODS." Poultry Science 63(5): 883-891.
Unrel	Thomas, J. M., L. L. Cadwell, et al. (1984). "CONCENTRATION OF ORALLY ADMINISTERED AND CHRONICALLY FED TECHNETIUM-95M IN JAPANESE QUAIL COTURNIX-JAPONICA EGGS." Health Physics 46(3): 657-664.
Bio acc, Surv	Thomas, P. A. (2000). "Radionuclides in the terrestrial ecosystem near a Canadian uranium mil - Part II: Small mammal food chains and bioavailability." Health Physics 78(6): 625-632.
HHE; Bio acc	Welford, G. A. and R. Baird (1967). "Uranium levels in human diet and biological materials." Health Phys 13(12): 1321-1324.

Note:

Reference citations are presented as obtained from the abstract review and have not been edited, and in some cases abbreviated. Full citations are available upon request.

Table A-5. Effect Group, Effect Type and Effect Measure used from U.S. EPA (2007d) in evaluating uranium toxicity literature.

BEHAVIOR (BEH) EFFECT GROUP	
General Behavior (BEH) Effect Type	
Effect Measure	Description
ACTP	accuracy of learned behavior
INST	induced sleeping time
LOCO	distance
NMVM	number of movements
Feeding Behavior (FDB) Effect Type	
Effect Measure	Description
CAIN	caloric intake
WCON	water consumption
BIOCHEMISTRY (BIO) EFFECT GROUP	
Biochemical (CHM) Effect Type	
Effect Measure	Description
BUNT	blood urea nitrogen
CHOL	cholesterol
CREA	creatine
GLUC	glucose
LPSA	lipid soluble antioxidants
PRTL	protein, total
RBCE	red blood cell
URIC	uric acide
VTD3	vitamin D3
Enzyme (ENZ) Effect Type	
Effect Measure	Description
ACHE	acetylcholinesterase
Hormone (HRM) Effect Type	
Effect Measure	Description
DOPA	dopamine
TSTR	testosterone
GROWTH (GRO) EFFECT GROUP	
Growth (GRO) Effect Type	
Effect Measure	Description
BDWT	body weight changes, non-adult organisms
Morphology (MPH) Effect Type	
	No effect measures from U.S. EPA (2007d) used

Table A-5. Effect Group, Effect Type and Effect Measure used from U.S. EPA (2007d) in evaluating uranium toxicity literature. (Continued)

MORTALITY (MOR) EFFECT GROUP	
Mortality (MOR) Effect Type	
Effect Measure	Description
GMOR	general mortality
MORT	mortality
SURV	survival
PHYSOLOGY (PHY) EFFECT GROUP	
Physiology (PHY) Effect Type	
	No effect measures from U.S. EPA (2007d) used
PATHOLOGY (PTH) EFFECT GROUP	
Gross Wasting (GRS) Effect Type	
Effect Measure	Description
BDWT	body weight changes, adult organisms
Organ Weight (ORW) Effect Type	
Effect Measure	Description
ORWT	organ weight changes
Histology (HIS) Effect Type	
Effect Measure	Description
GHIS	histological changes, general
GLSN	gross lesions
REPRODUCTION (REP) EFFECT GROUP	
Reproduction (REP) Effect Type	
Effect Measure	Description
ODVP	offspring development
ORWT	reproductive organ weight
OTHR	other (pathology, biochemistry, etc.) in offspring
PBEH	progeny behavior
PRFM	pregnant females in population
PROG	progeny counts/numbers
PRWT	progeny weight (TBWT, LTWT)
RHIS	reproductive organ histology
TERA	teratogenic measurements
TEWT	testes weight

Table A-6. Description of toxicological attributes used to score toxicology results based on U. S. EPA (2003b).

Attribute	Description
Data Source	10 = Paper is a primary data source, 0 = paper is not a primary source (paper rejected for use in TRV derivation.
Chemical Form	10 = Contaminant form is reported and is the same or similar to that found in the medium of concern. 5 = Contaminant form is reported but different from the medium of concern, or the form in the medium of concern is unknown. 4 = Contaminant form is not reported.
Test Concentration	10 = Contaminant concentration in test substance (i.e. food, drinking water) explicitly reported as actual measured values or unmeasured but analytically verified. 5 = Test substance concentration reported as nominal values (these may have been analytically verified but paper does not explicitly indicate). 1 = Test substance concentrations calculated. 0 =Test substance concentration not reported.
Dose Quantification	10 = Administered dose reported as mg per kg of body weight. 7 = Administered doses calculated but intake rates and body weights provided. 6 = Administered dose calculated but only one value (intake rate or body weight) provided. 5 = Administered doses calculated based on estimated intake rates and body weights. 0 = Administered doses cannot be calculated (study is rejected for use in TRV derivation).
Dose Range	10 = Both a NOAEL and LOAEL are identified and are within a factor of 3. 8 = Both a NOAEL and LOAEL are identified and are within a factor of 10. 6 = Both a NOAEL and LOAEL are identified abut are not within a factor of 10. 5 = Only a NOAEL is identified. 4 = Only an LOAEL is identified. 0 = Study lacks a suitable control group (study is rejected for use in TRV derivation).
Dose Route	10 = Dietary. 8 = Other oral, solid exposures (gavage, capsule). 5 = Other oral, liquid exposures. 0 = Not oral (study is rejected for use in TRV derivation.
Endpoint	10 = Endpoint in the Reproductive effect group. 9 = Endpoint in the Mortality effect group. 8 = Endpoint in the Growth effect group. 4 = Endpoint in the Pathology, Behavior or Physiology effect group. 1 = Endpoint in the Biochemical effect group.
Exposure Duration	10 = Exposure duration encompasses multiple generations of test species, exposure duration is at least 0.1 times the expected life span of the test species, or the exposure occurs during a critical life phase. 6 = Exposure duration is shorter than 0.1 times the expected life span of the test species but multiple dosing intervals occur. 3 = Exposure duration is shorter than 0.1 times the expected life span of the test species and only one dose interval occurs. 0 = Acute exposure or single oral dose (study rejected for use in TRV derivation).
Statistical Analysis	10 = Accepted statistical analysis used and described, the average, standard deviation and number of data points presented. 7 = Accepted statistical analyses used and described, the average, standard deviation and/or number of data points not presented. 5 = Statistical analysis apparently conducted but not described, the average, standard deviations and/or number of data points not presented. 3 = Statistical analysis not conducted, accepted evaluations procedures conducted and described. 0 = Statistical analysis not conducted, no description of evaluation presented.
Test Conditions	10 = Follows a standard guideline and reports all measurement parameters. 10 = Does not follow a standard guideline but reports all test parameters. 7 = Follows a standard guideline but does not report test parameters. 4 = Does not follow a standard guideline and reports some, but not all of the test parameters. 2 = Does not report any test parameters.

Table A-7. References used in the development of a mammalian TRV for uranium.

Ref #	Reference
1	Albina, M. L., M. Belles, V. Linares, D. J. Sanchez, and J. L. Domingo. 2005. Restraint stress does not enhance the uranium-induced developmental and behavioral effects in the offspring of uranium-exposed male rats. Toxicology 215(1-2): 69-79.
2	Arnault, E., M. Doussau, A. Pesty, B. Gouget, A. Van der Meeren, P. Fouchet and B. Lefevre. 2008. Natural uranium disturbs mouse folliculogenesis in vivo and oocyte meiosis in vitro. Toxicology 247(2-3): 80-87.
3	Belles, M., M. L. Albina, V. Linares, M. Gomez, D. J. Sanchez and J. L. Domingo. 2005. Combined action of uranium and stress in the rat. I. Behavioral effects. Toxicol Lett 158(3): 176-185.
4	Bensoussan, H., L. Grancolas, B. Dhieux-Lestaevel, O. Delissen, C. M. Vacher, I. Dublineau, P. Voisin, P. Gourmelon, M. Taouis and P. Lestaevel. 2009. Heavy metal uranium affects the brain cholinergic system in rat following sub-chronic and chronic exposure. Toxicology 261(1-2): 59-67.
5	Berradi, H., J. M. Bertho, N. Dudoignon, A. Mazur, L. Grandcolas, C. Baudelin, S. Grison, P. Voisin, P. Gourmelon and I. Dublineau. 2008. Renal anemia induced by chronic ingestion of depleted uranium in rats. Toxicol Sci 103(2): 397-408.
6	Briner, W. and K. Byrd. 2000. Effects of depleted uranium on development of the mouse. Metal Ions in Biology and Medicine 6: 459-461.
6	Briner, W. and B. Abboud. 2002. Behavior of juvenile mice chronically exposed to depleted uranium. Metal Ions in Biology and Medicine, Vol 7. L. Khassanova, P. Colleryet al. Montrouge, John Libbey Eurotext. 7: 353-356. (Duplicate data to Briner and Byrd, 2000).
7	Briner, W. 2002. Altered open-field performance in depleted uranium exposed rats. Metal Ions in Biology and Medicine, Vol 7. L. Khassanova, P. Colleryet al. Montrouge, John Libbey Eurotext. 7: 342-345.
8	Briner, W. and D. Davis. 2002. Lipid oxidation and behavior are correlated in depleted uranium exposed mice. Metal Ions in Biology and Medicine, Vol 7. L. Khassanova, P. Colleryet al. Montrouge, John Libbey Eurotext. 7: 59-63.
9	Briner, W. and J. Murray. 2005. Effects of short-term and long-term depleted uranium exposure on open-field behavior and brain lipid oxidation in rats. Neurotoxicology and Teratology 27(1): 135-144.
10	Briner W. 2009. Effects of depleted uranium on mouse midbrain catecholamines and related behavior. Internet Journal of Toxicology 7(1):No pp. http://www.ispub.com/journal/the_internet_journal_of_ toxicology/volume_7_number_2_29/article/effects-of-depleted-uranium-on-mouse-midbraincatecholamines-and-related-behavior.html. November 5, 2010.
11	Bussy, C., P. Lestaevel, B. Dhieux, C. Amourette, F. Paquet, P. Gourmelon and P. Houpert. 2006. Chronic ingestion of uranyl nitrate perturbs acetylcholinesterase activity and monoamine metabolism in male rat brain. Neurotoxicology 27(2): 245-252.
12	Domingo, J.L., A, Ortega, J. Paternain and J. Corbella. 1989b. Evaluation of the perinatal and postnatal effects of uranium in mice upon oral administration. Archives of Environmental Health 44 (6), 395–398.
13	Domingo, J.L., J.L. Paternain, J.M. Llobet and J. Corbella. 1989c. The developmental toxicity of uranium in mice. Toxicology 55, 143–152.
14	Feugier, A., S. Frelon, P. Gourmelon and M. Claraz. 2008. Alteration of mouse oocyte quality after a subchronic exposure to depleted Uranium. Reproductive Toxicology 26(3-4): 273-277.
15	Gilman, A. P., D. C. Villeneuve, V. E. Secours, A. P. Yagminas, B. L. Tracy, J. M. Quinn, V. E. Valli, R. J. Willes and M. A. Moss. 1998a. Uranyl nitrate: 28-day and 91-day toxicity studies in the Sprague-Dawley rat. Toxicological Sciences 41(1): 117-128.
16	Gilman, A. P., D. C. Villeneuve, V. E. Secours, A. P. Yagminas, B. L. Tracy, J. M. Quinn, V. E. Valli and M. A. Moss. 1998b. Uranyl nitrate: 91-day toxicity studies in the New Zealand white rabbit. Toxicological Sciences 41(1): 129-137.
17	Gilman, A. P., M. A. Moss, D. C. Villeneuve, V. E. Secours, A. P. Yagminas, B. L. Tracy, J. M. Quinn, G. Long and V. E. Valli. 1998c. Uranyl nitrate: 91-day exposure and recovery studies in the male New Zealand white rabbit. Toxicological Sciences 41(1): 138-151.

Table A-7. References used in the development of a mammalian TRV for uranium. (Continued)

Ref #	Reference
18	Goel, K.A., V.K. Garg and V. Garg. 1979. Histopathological Alterations Induced by Uranyl Nitrate in the Liver of Albino Rat. Bulletin of Environmental Contamination and Toxicology 22(6): 785-790.
18	Goel, K.A., V.K. Garg and V. Garg. 1980. Histopathology of kidney of albino rat poisoned with uranyl nitrate. Bull Environ Contam Toxicol 24:9-12. (Duplicate data to Goel et al. 1979).
19	Grignard, E., Y. Gueguen, S. Grison, J. M. A. Lobaccaro, P. Gourmelon and M. Souidi. 2008. Contamination with depleted or enriched uranium differently affects steroidogenesis metabolism in rat. International Journal of Toxicology 27(4): 323-328.
20	Hao, Y., R. Li, Y. Leng, J. Ren, J. Liu, G. Ai, H. Xu, Y. Su and T. Cheng. 2009. A study Assessing the Genotoxicity in Rats after Chronic Oral Exposure to a Low Dose of Depleted Uranium. Journal of Radiation Research 50(6): 521-528.
21	Hao, Y., R. Li, Y. Leng, J. Ren, J. Liu, G. Ai, H. Xu, Y. Su and T. Cheng. 2012. The Reproductive Effects in Rats after Chronic Oral Exposure to Low-dose Depleted Uranium. J Radiat Res 53(3): 377-384.
22	Houpert, P., P. Lestaevel, C. Amourette, B. Dhieux, C. Bussy and F. Paquet. 2004. Effect of U and 137Cs chronic contamination on dopamine and serotonin metabolism in the central nervous system of the rat. Can J Physiol Pharmacol 82(2): 161-166.
23	Houpert, P., P. Lestaevel, C. Bussy, F. Paquet and P. Gourmelon. 2005. Enriched but not depleted uranium affects central nervous system in long-term exposed rat. Neurotoxicology 26(6): 1015-1020.
24	Houpert, P., S. Frelon, P. Lestaevel, C. Bussy, P. Gourmelon and F. Paquet. 2007a. Parental exposure to enriched uranium induced delayed hyperactivity in rat offspring. Neurotoxicology 28(1):108-113.
25	Houpert, P., J. C. Bizot, C. Bussy, B. Dhieux, P. Lestaevel, P. Gourmelon and F. Paquet. 2007b. Comparison of the effects of enriched uranium and 137cesium on the behaviour of rats after chronic exposure. Int J Radiat Biol 83(2):99-104.
26	Kelada, I. P., A. S. Osman, G. M. Fouad and S. H. Radi. 2008. Experimental simulation for accidental exposure to uranium pollutants in drinking water. A histological study on the possible impact to the cerebral cortex of adult albino rats. Bull Alex Fac Med 44:253-60.
27	Kundt, M. S., C. Martinez-Taibo, M. C. Muhlmann and J. C. Furnari. 2009. Uranium in drinking water: effects on mouse oocyte quality. Health Physics 96(5): 568-574.
28	Lestaevel, P., C. Bussy, F. Paquet, B. Dhieux, D. Clarencon, P. Houpert and P. Gourmelon. 2005a. Changes in sleep-wake cycle after chronic exposure to uranium in rats. Neurotoxicology and Teratology 27(6): 835-840.
29	Lestaevel, P., E. Romero, B. Dhieux, H. Ben Soussan, H. Berradi, I. Dublineau, P. Voisin and P. Gourmelon. 2009. Different pattern of brain pro-/anti-oxidant activity between depleted and enriched uranium in chronically exposed rats. Toxicology 258(1): 1-9.
30	Linares, V., M. L. Albina, M. Belles, E. Mayayo, D. J. Sanehez and J. L. Domingo. 2005. Combined action of uranium and stress in the rat - II. Effects on male reproduction. Toxicol Lett 158(3): 186-195.
31	Linares, V., M. Belles, M. L. Albina, J. J. Sirvent, D. J. Sanchez and J. L. Domingo. 2006. Assessment of the pro-oxidant activity of uranium in kidney and testis of rats. Toxicol Lett 167(2): 152-161.
32	Linares, V., D. J. Sanchez, M. Belles, L. Albina, M. Gomez and J. L. Domingo. 2007. Pro-oxidant effects in the brain of rats concurrently exposed to uranium and stress. Toxicology 236(1-2): 82-91.
33	Linares, V., M. Belles, M. L. Albina, V. Alonso, J. L. Domingo and D. J. Sanchez. 2008. Chemical toxicity of uranium in mammals: a summary of some recent results. Metal Ions in Biology and Medicine 10: 601-608.
34	Llobet, J.M., J.J. Sirvent, A. Ortega and J.L. Domingo. 1991. Influence of chronic exposure to uranium on male reproduction in mice. Fundamental and Applied Toxicology16 (4), 821–829.
35	Mahmoudzadeh, A., E. Javadi and Z. Mohseni. 2007. Evaluation of changes of kidney parameteres in New Zealand rabbits subsequent to 90 days exposure to uranyl nitrate in drinking water. Iranian Journal of Public Health 36(4): 65-69.

Table A-7. References used in the development of a mammalian TRV for uranium. (Continued)

Ref #	Reference
36	Malenchenko, A. F., N. A. Barkun and G. F. Guseva. 1978. Effect of uranium on the induction and course of experimental autoimmune orchitis and thyroiditis. J Hyg Epidemiol Microbiol Immunol 22(3): 268-277.
37	Maynard, E.A., and H.C. Hodge. 1949. Studies of the toxicity of various compounds when fed to experimental animals. In: Voegtlin, I.C., Hodge, H.C. (Eds.), Pharmacology and Toxicology of Uranium Compounds. National Nuclear Energy Series 6. McGraw-Hill, New York,pp. 309–376.
37	Maynard, E. A., W. L. Downs and H.C. Hodge. 1953. Oral toxicity of uranium compounds. In Voegtlin, C. and Hodge, H. C., editors. Pharmacology and toxicology of uranium, Volume 3. New York, McGraw-Hill, 1221-1369. Note: This is a continued analysis of the data presented in Maynard and Hodge (1940).
38	McDonald-Taylor, C. K., M. K. Bhatnagar, A. Gilman, A. Yagminas and A. Singh. 1992. Uranyl nitrate-induced glomerular basement membrane alterations in rabbits a quantitative analysis. Bulletin of Environmental Contamination and Toxicology 48(3): 367-373.
39	Miller, A. C., M. Stewart, and R. Rivas. 2010. Preconceptional paternal exposure to depleted uranium: transmission of genetic damage to offspring. Health Physics 99(3): 371-379.
40	Ortega, A., J. L. Domingo, J. M. Llobet, J. M. Tomas and J. L. Paternain. 1989a. Evaluation of the oral toxicity of uranium in a 4-week drinking-water study in rats. Bulletin of Environmental Contamination and Toxicology 42(6): 935-941.
41	Ozmen, M. and M. Yurekli. 1998. Subacute toxicity of uranyl acetate in Swiss-Albino mice. Environmental Toxicology and Pharmacology 6(2): 111-115.
42	Paternain, J. L., J. L. Domingo, A. Ortega, and J. M. Llobet. 1989. The effects of uranium on reproduction, gestation, and postnatal survival in mice. Ecotoxicol. Environ. Saf. 17: 291-296.
43	Racine, R., L. Grandcolas, S. Grison, J. Stefani, O. Delissen, P. Gourmelon, G. Veyssiere and M. Souidi. 2010. Cholesterol 7 alpha-hydroxylase (CYP7A1) activity is modified after chronic ingestion of depleted uranium in the rat. Journal of Steroid Biochemistry and Molecular Biology 120(1): 60-66.
44	Raymond-Whish, S., L.P. Mayer, T. O'Neal, A. Martinez, M.A. Sellers, P.J. Christian, S.L. Marion, C. Begay, C.R. Propper, P.B. Hoyer and C.A. Dyer. 2007. Drinking water with uranium below the US EPA water standard causes estrogen receptor-dependent responses in female mice. Environmental Health Perspectives 115(12): 1711-1716.
45	Rouas, C., J. Stefani, S. Grison, L. Grandcolas, C. Baudelin, I. Dublineau, M. Pallardy and Y. Gueguen. 2011. Effect of nephrotoxic treatment with gentamicin on rats chronically exposed to uranium. Toxicology 279(1-3): 27-35.
46	Sanchez, D. J., M. Belles, M. L. Albina, M. Gomez, V. Linares and J. L. Domingo. 2006a. Exposure of pregnant rats to uranium and restraint stress: effects on postnatal development and behavior of the offspring. Toxicology 228(2-3): 323-332.
47	Souidi, M., Gueguen, Y., C. Lindard, N. Dudoignon, S. Grison, C. Baudelin, C. Marguette, P. Gourmelon, J. Aigueperse and I. Dublineau. 2005. In vivo effects of chronic contamination with depleted uranium on CYP3A and associated nuclear receptors PXR and CAR in the rat. Toxicology 214: 113-122.
48	Taulan, M., F. Paquet, C. Maubert, O. Delissen, J. Demaille and M. C. Romey. 2004. Renal toxicogenomic response to chronic uranyl nitrate insult in mice. Environmental Health Perspectives 112(16): 1628-1635.
49	Tissandie, E., Y. Gueguen, J. M. A. Lobaccaro, L. Grandcolas, P. Voisin, J. Aigueperse, P. Gourmelon and M. Souidi. 2007. In vivo effects of chronic contamination with depleted uranium on vitamin D-3 metabolism in rat. Biochimica Et Biophysica Acta-General Subjects 1770(2): 266-272.
50	Wade-Gueye, N. M., O. Delissen, P. Gourmelon, J. Aigueperse, I. Dublineau and M. Souidi. 2012. Chronic exposure to natural uranium via drinking water affects bone in growing rats. Biochimica Et Biophysica Acta-General Subjects 1820(7): 1121-1127.

Attachment A

Responses to Regulatory Comments

Regulatory Comments and DOE/LLNL Responses for the Mammalian and Avian Toxicity Reference Values for use in the Building 812 Baseline Ecological Risk Assessment at Lawrence Livermore National Laboratory Site 300

U.S. Environmental Protection Agency (U.S. EPA) Comments

Comments dated January 25, 2013

U.S. EPA GENERAL COMMENT

1. The document adequately describes the toxicity data compiled from the published literature which will be needed to complete the ecological risk assessment for Site 300. The document identifies and selects appropriate receptors to help evaluate the potential impact of the Site contaminants of concern as approved by the agencies overseeing this process. While the more common contaminants already have Toxicity Reference Values (TRVs) published and approved by the agencies, uranium and its various forms do not. This effort mostly involved developing bird and mammal TRVs for uranium using methods developed by the EPA and accepted by others working in this field. The uranium TRVs, as presented, are acceptable based on the amount of data surveyed and the approach used to evaluate these data. No further effort is required to finalize the TRVs.

DOE/LLNL Response:

DOE/LLNL appreciates the U.S. EPA's concurrence on this document.

Department of Toxic Substance Control (DTSC) Ecological Risk Assessment Section (ERAS) Comments

Comments dated December 27, 2012

DTSC GENERAL COMMENTS

1. ERAS does have some comments on the Mammalian and Avian Toxicity Reference Values for the Building 812 Baseline Ecological Risk Assessment at LLNL Site 300. These comments are presented in the Specific Comments below.

DOE/LLNL Response:

It should also be noted that the DTSC response Background sentence that states "Major research was conducted on the properties and behavior of plutonium" is not correct. Plutonium was not used at Site 300.

DTSC SPECIFIC COMMENTS

1. Page 5 of 10, Mammalian Toxicity Reference Value. The sentence 'Further review of Figure 2 shows that a value of 1 mg/kg/d would be higher than all bound NOAEL/LOAEL results except for the mortality result from Domingo et al. (1989b) appears to be misstated. It seems 'lower' should replace 'higher' in the sentence.

The 1 mg/kg/day for uranium is the lowest bounded NOAEL for growth and is less than the geometric mean and therefore appears to be a conservative estimate of a uranium NOAEL TRV and is acceptable to ERAS. Please explain why the report is not also proposing a LOAEL-based TRV.

DOE/LLNL Response:

DOE/LLNL agrees the word "higher" in the above reference sentence should be "lower" and will change the document accordingly.

The TRVs developed for the Building 812 baseline ecological risk assessment generally followed the approach developed by the U.S. EPA for the development of ecological soil screening levels. The specific methods for developing the TRVs are outlined in Attachments 4-2 through 4-5 to the Guidance for Developing Ecological Soil Screening Levels (U.S. EPA, 2003a,b and U.S. EPA, 2007d,e, references as cited in original TRV document). In Attachment 4-5 (U.S. EPA, 2007e), the U.S. EPA describes several methods that were considered in developing the TRVs, including the critical study approach (in which a relevant NOAEL or LOAEL is used from a critical study), benchmark dose approach, distributional approaches, and the weight-of-evidence approach. The weight-of-evidence approach was selected as it uses all relevant and appropriate NOAEL and LOAEL data, which are then plotted and examined to identify a threshold that would be protective. Thus, it avoids reliance on a critical study and does

not require the use of safety factors. However, it does require a relatively large data set. The minimum data set established by the U.S. EPA is at least three NOAEL or LOAEL results for at least two species for the growth, reproduction, or mortality effects. Since both NOAEL and LOAEL data are considered in the selection of the proposed TRV, selection of a separate NOAEL TRV and LOAEL TRV is not necessary.

2. Page 6 of 10, Avian Uranium TRV. ERAS agrees that, based on the evidence provided in the report, there is insufficient data to develop an avian uranium TRV. The report states 'Therefore, it appears that birds are not critical vertebrates for effects of uranium'. General statements that birds are not as sensitive to uranium as mammals should not be made based on a single study with a single species. The assumption could be true but not based on the evidence provided in the report. Further, for this comparison to be made the toxicity tests should be based on comparison of like studies between birds and mammals (i.e., acute/acute; chronic/chronic), however it appears the report is comparing an acute study in birds to chronic studies in mammals. The conclusion of 10 mg/kg/day based on 10 times the mammalian TRV of 1 mg/kg/day is nebulous. In ERAS' opinion it would be better not to propose an avian TRV at all and instead assume that estimation of hazard for the protection of mammals is likely protective of birds and state that in the work plan and risk assessment.

DOE/LLNL Response:

The statement "Therefore, it appears that birds are not critical vertebrates for effects of uranium" comes from the study by Harvey et al. (1986) in which they compared the acute effects of uranium in leghorn chick to similar acute studies conducted on rats and mice, and found the highest non-lethal dose to chicks was 100 fold higher than that observed for rats and mice. Therefore, similar acute studies were compared. DTSC is correct that data are available only from a single study on a single bird species (leghorn chicks), and thus is limited. However, the conclusion that birds are less sensitive to uranium as compared to mammals is further supported by the oral feeding study conducted on black ducks reported on by Haseltine and Silo (1983), which found a NOAEL of 160 mg/kg/d. This NOAEL is 160 times the currently proposed mammalian TRV of 1 mg/kg/d. Thus, based on the limited data available, the statement is reasonable. DOE/LLNL agrees to modify the statement to read "Therefore, based on relatively limited data, it appears that birds are not as sensitive to the effects of uranium as compared to mammals".

For the reasons described above in the response to Specific Comment 1, the weight-of-evidence approach could not be strictly used to develop an avian TRV for uranium due to the limited data set. Rather, the critical study approach was used. This was the method used by Sample et al. (1996) in developing an avian TRV for uranium. The critical study is that of Haseltine and Silo (1983). Sample et al. (1996) applied a safety factor of 0.1 to the NOAEL of 160 mg/kg/d,

resulting in a TRV of 16 mg/kg/d. DOE/LLNL is proposing a TRV of 10 mg/kg/d, which is based on this critical study, as well as assuming birds are only 10 times less sensitive to uranium than mammals, rather than the 100 times as suggested by Harvey et al. (1986), adding for a further measure of safety.

DOE/LLNL is not clear by what DTSC means in suggesting that the estimation of hazard and protection of mammals is likely protective of birds. Is DTSC suggesting that DOE/LLNL not conduct a hazard evaluation on birds, relying solely on the mammalian hazard evaluation? Or is DTSC suggesting using the 1 mg/kg/d mammalian TRV on birds? DOE/LLNL agrees the toxicity data on birds is very limited. However, the available data strongly suggests using the mammalian TRV on birds would be overly conservative, and thus it would be inappropriate to use in the bird hazard evaluation. While DOE/LLNL would consider dropping the bird evaluation, DTSC should recognize that the selected bird species, the rock wren, has a much larger range (both breeding territory and home range), and a substantially different diet (a nearly strict insectivore), compared to the deer mouse. Thus, DOE/LLNL believes evaluating the rock wren using a TRV of 10 mg/kg/d would provide useful information to decision makers determining the best course of action with respect to remediation alternatives for the Building 812 operable unit, and proposes retaining the rock wren evaluation using an avian TRV of 10 mg/kg/d. DOE/LLNL does agree that the uncertainties in this analysis, including the limited bird toxicity data available, should be discussed in the risk characterization portion of the baseline risk assessment.

3. Figures 1 and 2. Please explain what the LOAEL values shown in the right hand portions of the graphs represent.

DOE/LLNL Response:

Using the protocol developed by the U.S. EPA (U.S. EPA, 2007e), each NOAEL and LOAEL data point is assigned a result number, corresponding to a specific experiment described in a specific paper. Table 1 shows the result number in the first column. For a given endpoint, a specific paper may have more than one result, if, for example, multiple experiments were performed using different species, exposure durations, or forms of uranium. Results from each experiment could be reported as a NOAEL, a LOAEL, or both. Result numbers are assigned by sorting the data within each endpoint so that the lowest NOAEL data point is assigned a result number of 1, with result numbers increasing as the NOAEL increases. Once all the NOAEL data are assigned a result number, experiments only reporting LOAEL data are assigned results numbers, again starting with the lowest LOAEL data point. Figures 1 and 2 are generated by plotting the NOAEL and LOAEL data by result number. This produces a graph in which the NOAEL data are plotted on the left, and the LOAEL data with no corresponding NOAEL data are plotted on the right. LOAEL data that have corresponding NOAEL data are plotted above the corresponding NOAEL data

point, and joined by a bar to show they come from the same experiment. These are what the U.S. EPA terms "bound" NOAEL/LOAEL results.

All references are as cited in original TRV document.

Comments dated April 11, 2013

DTSC RESPONSE TO GENERAL COMMENT 1

Comment noted.

DTSC RESPONSE TO SPECIFIC COMMENTS

1. ERAS does not understand the final sentence in the above selection. If the calculated hazard exceeds unity based on the no effect TRV (NOAEL TRV) what will this mean? Will an effect level TRV (LOAEL TRV) then be developed and a hazard quotient estimated based on the LOAEL TRV?

DOE/LLNL Response:

If the hazard quotient exceeds unity based on the proposed mammalian TRV, this suggests the potential for ecological hazard exists. At this point, the baseline ecological risk assessment moves from hazard estimation to risk characterization. It is during this process that uncertainties in the hazard estimation process are discussed. DOE/LLNL agrees that the proposed mammalian uranium TRV is based primarily on NOAEL data, although LOAEL data were considered. Thus, DTSC has a valid point that a hazard quotient exceeding one does not necessarily indicate ecological harm will occur, but simply has the potential to occur. During the risk characterization process, consideration of the magnitude of the hazard quotient and the data upon which the TRV is based would be appropriate. This also includes the TRVs for copper, lead, nickel and zinc. Additional exposure modeling based on a TRV that would clearly result in an ecological effect (i.e., a TRV based primarily on LOAEL data) could provide additional useful information to the decision makers. Whether to conduct such additional analysis will be discussed with, and agreed upon by, all the regulatory agencies at the scientific/management decision point.

2. ERAS will not disagree with the proposed avian NOAEL TRV, given that the uncertainties in its estimate will be discussed in the uncertainty section. ERAS is not suggesting using the mammalian TRV of 1 mg/kg/day for avian receptors. The ERAS suggestion that uranium TRV may not be needed to be developed from such limited data, was based on the simple observation that the proposed home range of the rock wren is 40 times greater than that of the deer mouse and that the rock wren TRV is 10 times greater than the deer mouse TRV. Less site fidelity equates to less exposure and the 10 fold greater avian TRV generally equates to a greater media concentration needed to effect a similar magnitude of toxicological effect (if bioavailability is similar). However, ERAS agrees with the DOE/LLNL response that difference in diet could be a significant component to influence the receptor specific magnitude of exposure. ERAS concurs with the use of the proposed avian uranium TRV in the ecological risk assessment.

DOE/LLNL Response:

DOE/LLNL appreciates the DTSC's concurrence on this point, and will proceed with the rock wren evaluation using the proposed avian TRV.

3. Thank you for the explanation, comment noted.

DTSC CONCLUSIONS

Based on the DOE/LLNL responses, ERAS waives its objection to using the proposed avian NOAEL. If uranium hazard quotients exceed unity, a LOAEL based TRV will need to be presented.

DOE/LLNL Response:

DOE/LLNL will proceed with the avian hazard evaluation using the proposed avian TRV.

Should uranium or other heavy metal hazard quotients exceed unity, DOE/LLNL agrees during the scientific management decision point to discuss with all the regulatory agencies the value in developing clearly LOAEL-based TRVs and reevaluating hazard using a LOAEL-based TRV.

Regional Water Quality Control Board (RWQCB)-Central Valley Region Comments

The RWQCB did not have any comments and deferred to the U.S. EPA and DTSC.

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Lawrence Livermore National Security, LLC • Livermore, California • 94551