April 16, 2000

UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMMISSION

BEFORE THE COMMISSION

In the Matter of:	)	
HYDRO RESOURCES, INC. P.O. Box 15910 Rio Rancho, New Mexico 87174	)	Docket No. 40-8968-ML

DECLARATION OF DR. JOHN D. FOGARTY IN SUPPORT OF INTERVENORS' REPLY TO THE NRC STAFF'S RESPONSE TO ENDAUM'S AND SRIC'S MOTION TO REOPEN AND SUPPLEMENT THE RECORD

I, John D. Fogarty, upon penalty of perjury, submit this declaration on behalf of Eastern Navajo Diné Against Uranium Mining ("ENDAUM") and the Southwest Research and Information Center ("SRIC") in support of the Intervenors' reply to the Nuclear Regulatory Commission ("NRC") Staff's Response ("Staff Response") to ENDAUM's and SRIC's Motion to Reopen and Supplement the Record (March 15, 2000) ("Motion to Reopen") of this proceeding related to licensing of Hydro Resources, Inc.'s ("HRI's"), Crownpoint Uranium Solution Mining Project ("CUP").

1. My name is John D. Fogarty. I am a family practice physician at the Crownpoint Healthcare Facility, a U.S. Indian Health Service hospital located in Crownpoint, N.M. I reside in Crownpoint, where I have lived since August 1999.

2. I am qualified and competent to make this declaration, and the factual statements

EXHIBIT
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herein are true and correct to the best of my knowledge, information and belief. The opinions expressed herein are based on my best professional judgment.

3. The purpose of this declaration is to reply to the comments and criticisms of the testimony I gave in an affidavit dated March 1, 2000 ("Fogarty March 1 Affidavit") by counsel for the NRC Staff and by Mr. Christepher McKenney of the NRC Staff. See Motion to Reopen, Exhibit 1. The responses of the NRC Staff and Mr. McKenney are contained in the NRC Staff's Response to Motion to Reopen and Supplement the Record (April 4, 2000) ("Staff Response") and the affidavit of Christepher A. McKenney (April 4, 2000) ("McKenney Affidavit"), which was attached to the Staff Response as Staff Exhibit 1.

4. I have reviewed the Staff Response and the McKenney Affidavit in great detail, and have re-reviewed several of the scientific studies and papers I submitted with my March 1 Affidavit and other relevant literature on uranium nephrotoxicity. On whole, nothing in the Staff Response or Mr. McKenney's affidavit dissuaded me from concluding that the uranium groundwater restoration standard of 0.44 milligrams per liter ("mg/L"), as set forth in Condition 10.21 of the HRI license, is not safe to protect public health in Church Rock or Crownpoint. The NRC Staff and its principal scientific witness, Mr. McKenney, continue to deny the importance and implications of recent scientific studies that demonstrate that a level of 0.44 mg/L of uranium in drinking water is unsafe for human consumption. It is quite clear from the available animal and human data that such a high level of uranium in drinking water almost certainly will lead to some form of kidney impairment as a result of chronic ingestion. I remain convinced that as long as NRC continues to authorize HRI, through its operating license, to maintain such a high uranium level in the Church Rock and Crownpoint groundwater after mining is concluded, the

CUP poses an unreasonable risk to the health and safety of the people of Crownpoint and Church Rock.

5. The Staff Response states that the "safety of using the 0.44 mg/L level as the secondary groundwater restoration goal for uranium was fully evaluated during the Staff's preparation of the FEIS. No showing is made which casts any doubt on the validity of the Staff's analysis in the FEIS." I disagree. The purpose of my March 1 Affidavit was to show that, regardless of the "evaluation" contained in the *Final Environmental Impact Statement*, the 0.44 mg/L restoration standard is inadequate to protect public health and safety. I will comment briefly on a few of the examples from the FEIS that were cited by the Staff and Mr. McKenney to reach their conclusions.

6. First, the FEIS noted that "[a] value of 300 pCi/mL [sic; the units should have been picoCuries per liter, or pCi/L] (0.44mg/L) would be used for uranium. This concentration was obtained from 10 CFR Part 20; it is suitable for unrestricted release of natural uranium to water and is below the State of New Mexico primary drinking water standard for uranium." FEIS at 4-27; cited in McKenney Affidavit at 1. As I indicated in my March 1 Affidavit (at 8-9), the 300 pCi/L "release" standard in 10 CFR 20 Appendix B is based on radiological properties of uranium, not on its chemical toxicity properties. These standards were *wrongly applied* to the Crownpoint Uranium Project.[1] In the CUP, solution mining would take place in a regional

[1]The FEIS's citation of the New Mexico "drinking water standard for uranium" was also wrongly applied and factually wrong. New Mexico has no "drinking water standard for uranium." The 5 mg/L "standard" to which the FEIS refers is contained in the New Mexico Water Quality Control Commission Regulations (¶ 3103.A) and is applicable to protection of groundwater from discharges onto or below the surface of the ground. Mr. McKenney repeated this factual error, and the inappropriateness of its application, when he mentioned that the "State

aquifer that is the sole source of drinking water for thousands of Navajo people in the Church Rock and Crownpoint areas and that contains groundwater having native uranium concentrations ranging from 1 μg/L (microgram per liter) to 7 μg/L, and averaging between 1 and 2 μg/L. Fogarty March 1 Affidavit at 7-8; see also, FEIS at 3-26 and 3-36, and Affidavit of Dr. Richard Abitz in support of ENDAUM's and SRIC's presentation on groundwater protection issues (January 8, 1999) at 10-16.

7. The other citations to the FEIS (e.g., 4-45 to 4-48 and 4-87) that Mr. McKenney and the Staff use to support their view that the FEIS adequately evaluated the 0.44 mg/L restoration standard recite the NRC's 10 CFR Part 20, Appendix B "effluent concentration limits" (to use Mr. McKenney's terminology at 3 of his affidavit.). There is no explanation in the FEIS of how the 300 pCi/L release limit applies to uranium's chemical toxicity, nor any justification that the level is safe for human consumption, other than the fact it is already codified in another NRC regulation. Hence, my criticism of the FEIS for its lack of biomedical evaluation of the 0.44 mg/L uranium restoration standard was correct: contrary to the conclusions of counsel for the Staff and Mr. McKenney, there was no such evaluation in the FEIS.[2]

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of New Mexico water quality standard for uranium is 5 mg/L." McKenney Affidavit at 2. That the 0.44 mg/L restoration standard for the CUP is "below" the New Mexico groundwater standard does not make the restoration standard safe.

[2]For the same reasons, neither does Mr. McKenney's recitation of EPA's 2 mg/L standard for surface water discharges subject to NPDES (National Pollutant Discharge Elimination System) permits make the case for the safety of the 0.44 mg/L restoration level. McKenney Affidavit at 2. The EPA's NPDES limitations address only surface water quality and have nothing to do with drinking water quality or human health risks associated with drinking water. Again, just because the 0.44 mg/L restoration level is less than the EPA NPDES discharge limitation does not make the restoration level safe.

8. Mr. McKenney is explicit that "uranium's chemical toxicity was not taken into account when establishing the Appendix B concentration levels." McKenney Affidavit at 4. He said he reviewed studies referenced in the EPA's Integrated Risk Information System (IRIS) to "verify that chemical toxicity was not a limiting factor for ingestion of uranium by members of the public." Id. He then recites the purpose of EPA's "chronic oral exposure figure", or reference dose (RfD), and concludes that the 10 CFR 20 Appendix B "effluent concentration limit" for uranium of 300 pCi/l "is within the uncertainty associated with the RfD." Id. at 5. He adds two more conclusions: first, that a "secondary groundwater restoration goal for uranium of 0.44 mg/L would result in minimal impacts to any future population" and therefore was "an acceptable limit to use in HRI's license. . ." (id. at 5), and second, that the 0.44 mg/L level "minimizes. . .or avoids all nephrotoxic effects. . ." Id. Mr. McKenney offers *no scientific explanation or analysis* to support these conclusions. He does not review the history of the EPA RfD for uranium, including the studies upon which it is based, nor attempt to back-calculate a maximum contaminant level for uranium to determine if the 0.44 mg/L level is a safe level for human consumption.

9. In the absence of such an analysis by Mr. McKenney, I applied the RfD contained in the IRIS database to a formula used by the World Health Organization ("WHO") and Health Canada to calculate a maximum contaminant level for uranium in drinking water. I did this to determine if, as Mr. McKenney asserts, the 0.44 mg/L restoration standard "is within the uncertainty associated with the RfD." McKenney Affidavit ¶ 8 at 5. My analysis, which is described in detail in the paragraphs that follow, shows that the 0.44 mg/L restoration standard is not within the range of uncertainty contemplated by EPA's RfD.

10. An RfD is an estimate of the daily amount of a substance that a person can ingest without having a high risk of experiencing a health effect during his or her lifetime. As a general matter, an RfD is derived from laboratory experiments in which large doses of a substance are administered to animals and the effects of that exposure are observed. This is exactly how the current EPA RfD for uranium was derived — from animal studies reported by Maynard and Hodge in their oft-cited 1949 paper, "Studies of the toxicity of various uranium compounds when fed to experimental animals." The Maynard and Hodge paper is summarized in the same IRIS summary of uranium toxicity that Mr. McKenney reviewed. For the record, I've attached as **Exhibit A** to this declaration a printout of that summary from EPA's IRIS website.

11. The oral RfD for soluble uranium given in the EPA IRIS summary is 0.003 milligrams (mg) per kilogram (kg) of body weight (bw) per day (d). This value is derived from the lowest observed adverse effect level ("LOAEL") of 2.8 mg/kg-bw/day, which Maynard and Hodge reported in their 1949 study of rabbits exposed to relatively high doses of uranium compounds for 30-day periods. The RfD is calculated by dividing the LOAEL by an uncertainty factor of 1,000, which consists of factors of 10 each for intraspecies variability, interspecies variability, and use of an LOAEL from an animal study. See **Exhibit A** at 4.

12. To test Mr. McKenney's conclusion that the 0.44 mg/L restoration standard written into HRI's license "is within the uncertainty associated with the RfD," and therefore presumably safe, I applied the analysis technique used by Michele Giddings in her chapter on uranium in the 1998 WHO drinking-water guideline document that I excerpted in my March 1 affidavit (see, Fogarty Exhibit I at 91) and used by Health Canada in its January 1999 background technical document on a revised uranium drinking water guideline (id., Exhibit H at 12). In both of these

papers, the revised maximum contamination level ("MCL") guideline for uranium in drinking water is derived from following formula:

$$MCL = \frac{TDI \times bw \times AF}{WC} \qquad \text{[Equation 1]}$$

where,

TDI = Tolerable Daily Intake (in mg/kg-bw/d)
bw = body weight (in kg)
AF = allocation factor (unitless), or the percentage of uranium intake derived from drinking water
WC = a person's daily water consumption, in liters (L)

Giddings' TDI is synonymous with EPA's RfD. The TDI differs from the RfD only in that it contains an uncertainty factor of 100 (for intra- and interspecies variability), or 10 times less than EPA's uncertainty factor of 1,000. Id., Exhibit I, at 91. Using EPA's RfD for uranium and Giddings' values for bw (60 kg), AF (0.1 or 10%), and WC (2 L/d), a theoretical uranium MCL can be calculated as follows:

$$MCL = \frac{0.003 \text{ mg/kg-bw/d} \times 60 \text{ kg} \times 0.1}{2 \text{ L/d}} = 0.009 \text{ mg/L, or } 9.0\ \mu\text{g/L} \qquad \text{[Equation 2]}$$

Hence, using EPA's own RfD and WHO's assumptions about body weight, allocation factor and average daily water consumption, results in an MCL "guideline" of 0.009 mg/L, or 9 μg/L — nearly 50 times *less* than NRC's restoration standard for the Crownpoint Project. Clearly, the 0.44 mg/L restoration goal is not within the range of uncertainty contemplated by EPA's RfD.

13. There is reason to believe, however, that EPA's RfD no longer reflects current scientific knowledge of the lowest effect level for uranium. As discussed in my March 1 affidavit, five modern studies (Mao, 1995; Limson-Zamora, 1998; and Gilman, 1998a, b and c) call into question Mr. McKenney's conclusions and the NRC's 0.44 mg/L restoration level. See

Fogarty March 1 Affidavit at 11-16 and Exhibits B, C, D, E and F. Initiatives by agencies such as WHO and Health Canada to *lower* their existing drinking water guidelines for allowable levels of uranium *are based largely* on the results of these five studies. Id. at 16-20 and Exhibits G, H and I. These agencies have recommended levels that are one to two orders of magnitude lower than the 0.44 mg/L level that Mr. McKenney concludes "avoids all nephrotoxic effects."

14. As I explained in my March 1 affidavit, the studies relied on by the NRC Staff, and used by EPA to derive an RfD for uranium, such as the Maynard and Hodge paper from 1949, are outdated and methodologically flawed. By its own admission, the EPA RfD has not been updated since October 1989. See **Exhibit A** at 1 and 6. EPA, therefore, could not have used data from any of the recent studies in developing the 0.003 mg/kg-bw/d RfD for uranium.

15. Gilman's recent animal studies demonstrated adverse effects on the kidneys of rats at dose equivalents as low as 0.06 mg/kg-bw/d. See Fogarty March 1 Affidavit, Exhibit D at 117. Both Health Canada and WHO not only cited Gilman's animal studies, but used the study's LOAEL for rats of 0.06 mg/kg-bw/d as the basis for a revised TDI, or RfD. Id., Exhibit H at 7-10; Exhibit I at 91. WHO, again using an uncertainty factor of only 100 instead of 1,000 to obtain a revised TDI of 0.0006 mg/kg-bw/d, calculated a maximum contaminant level of 2 μg/L, which it said "would be protective based on associations for subclinical renal effects reported in preliminary epidemiological studies." Id., Exhibit I at 91. The value of 2 μg/L is 240 times less than the NRC groundwater restoration standard for the Crownpoint Project. WHO has adopted this level as its international guideline for maximum levels of uranium in drinking water.

16. The studies by Gilman, et al., in the late-1990s generated better measures of uranium's nephrotoxic effects than those conducted by Maynard and Hodge in 1949. First,

Gilman and colleagues studied uranium's effects for 91 days, or three times longer than Maynard and Hodge. This longer study period has important implications, according to Giddings' summary in the WHO guidelines paper:

> "There is some evidence that tolerance may develop following repeated exposure to uranium. . . .This tolerance does not, however, prevent chronic damage to the kidney, as the regenerated cells are quite different; although histopathologically it may appear that the repair process is well advanced, the urinary biochemical changes return to normal only slowly. . . .Persistent ultrastructural changes in the proximal tubules of rabbits have also been reported to be associated with the kidney's ability to store uranium. . . .Cell damage in the proximal tubules was significantly more severe in animals allowed up to a 91-day recovery period than in animals in the no-recovery group."

Fogarty March 1 Affidavit, Exhibit I at 86 (citations in original text omitted). And second, Maynard and Hodge did not measure urinary glucose to gauge kidney damage, as did Gilman and colleagues. As I discussed in my March 1 affidavit, elevated urinary glucose is a sensitive biomarker of damage in the proximal tubules of the kidney. Id. at 11-16. Gilman and colleagues also observed lesions in the kidney tubules of male rats fed water containing 0.96 mg/L uranyl nitrate hexahydrate. Id., Exhibit D at 117. This concentration was the lowest level administered to the rats and is equivalent to 0.06 mg-U/kg-bw/d, or the dose now used by Health Canada and WHO in revising their drinking water guidelines downward.

17. In summary, then, the uranium cleanup standard for the Crownpoint Project does not have an ample margin of safety, even when EPA's outdated uranium RfD is used to calculate a maximum contaminant level. When the lower uranium LOAEL derived from Gilman's studies is used to calculate an MCL, the magnitude of the inadequacy of the cleanup standard advanced by Mr. McKenney and the NRC Staff is magnified even more.

18. The environmental context in which the Crownpoint Uranium Project is proposed has

important health implications. The vast majority of people in Church Rock and Crownpoint have only one source of drinking water — groundwater. Health Canada noted in its January 1999 drinking water guideline notice that people in rural areas obtain much of their drinking water from groundwater sources, which have generally higher uranium levels than surface water sources. See Fogarty Affidavit, Exhibit H at 3-4, 12. Limson-Zamora et al. (1998) found that water contributed between 31% and 98% of total daily uranium intake for individuals whose drinking water came from wells. Id., Exhibit C at 71. The fact that people in Church Rock and Crownpoint could get a higher proportion of their daily intake of uranium from groundwater magnifies the need a lower restoration level.

19. Mr. McKenney alludes to a note in 10 CFR 20, Appendix B, that requires a licensee to limit the soluble uranium intake by an individual to 10 mg in a week (or, on average, 1.43 mg/d) "in consideration of chemical toxicity." 10 CFR 20.1201(e). While it is unclear to me whether or how this limit is applied in the context of the CUP, it is patently not safe. In the Limson Zamora study (Fogarty March 1 Affidavit, Exhibit C at 73), abnormally high levels of urinary glucose and alkaline phosphatase where observed in people who had total daily uranium intakes ranging from 21-410 μg and 220-410 μg. In other words, biomarkers indicating damage to the proximal tubules of the kidneys were evident in people who consumed from 3.5 times to 68 times *less* uranium than NRC would require a licensee to "limit" on average every day.

20. In his April 4 affidavit, Mr. McKenney chooses to comment only on the Mao, et al., study from 1995. He ignored the Limson-Zamora and Gilman studies, and has nothing to say about the recommendations of USEPA, CalEPA, Health Canada and WHO and the scientific bases for those recommendations. Instead, he criticizes the Mao study by commenting on its

small sample size, the difficulty in proving cause and effect, and the difficulty in quantifying exposure. I agree with Mr. McKenney that the Mao study is limited by these factors inherent in the study design. However, as a population-based study looking at the effects of chronic uranium ingestion on kidney function, it has received the attention of regulatory and health institutions worldwide because it shows a correlation between composite uranium intake in drinking water and increasing levels of microalbuminuria in exposed subjects. Fogarty March 1 Affidavit at 12-13 and Exhibit B.

21. Mr. McKenney concludes with a quote from the Mao paper that "a similar study with more precise exposure data and greater sample size to increase statistical power would be a logical extension to that presented." I agree that additional epidemiological studies on this issue are needed. However, the need for additional studies is irrelevant to the issue of the safety of the 0.44 mg/L restoration standard. As I have demonstrated, the standard is not safe to protect human health in Church Rock and Crownpoint.

22. Finally, water is not the only medium by which people can be exposed to uranium. As discussed in the papers by Health Canada (id., Exhibit H at 3-4) and WHO (id., Exhibit I at 83-84), uranium contained in meats and edible plants also contributes to the total daily intake. The meat pathway is particularly relevant in the Church Rock area where animals that drank from streams receiving uranium mine discharge water had significantly higher levels of uranium in their edible muscle and organs than control animals that grazed and drink in non-uranium producing areas. See Written Testimony of Dr. Christine J. Benally in support of ENDAUM's and SRIC's presentation on environmental justice issues (February 15, 1999) at 41-42, and Exhibits U and V attached thereto. Neither Mr. McKenney in his most recent affidavit nor the

NRC Staff in the FEIS evinced any knowledge of the animal uptake studies done in the New Mexico uranium districts in the mid-1980s. Nor have they shown any overt interest in verifying the safety of their uranium restoration standard by undertaking a scientifically credible analysis of total daily uranium intake in the affected communities of Church Rock and Crownpoint.

23. In summary, the secondary groundwater restoration standard for uranium for the Crownpoint Project poses an exceptionally grave risk to the health and safety of the thousands of Navajo people who use the water resources of the Westwater Canyon Aquifer. The information provided in my March 1 affidavit and reviewed again in his declaration provides convincing evidence that the standard is wholly unsafe. Without scientific reason or analysis, the NRC Staff continues to disregard the findings of the recent studies on the health effects of uranium in drinking water and continues, unreasonably in my view, to rely on an inappropriate radiation regulation applied in the wrong context. Additionally, the NRC Staff now appears to be alone among health and environmental agencies in clinging to an unsafe, outdated and unsubstantiated restoration standard. The Commission can and should overrule the Staff on this critical issue and accept this new and compelling data on uranium nephrotoxicity before mining begins.

24. This concludes my testimony.

AFFIRMATION

I declare on this 16th day of April 2000 at Albuquerque, New Mexico, under penalty of perjury that the foregoing is true and correct to the best of my knowledge, and the opinions expressed herein are based on my best professional judgment.

John D. Fogarty, M.D.

EPA United States Environmental Protection Agency

IRIS
Integrated Risk Information System

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0421
Uranium, soluble salts; no CASRN

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Uranium, soluble salts

File On-Line 10/01/1989

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	10/01/1989
Inhalation RfC Assessment (I.B.)	no data	

Attachment A

Carcinogenicity Assessment (II.) no data

_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Uranium, soluble salts
CASRN --
Last Revised -- 10/01/1989

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Initial body weight loss; moderate nephrotoxicity 30-Day Oral Rabbit Bioassay (diet) Maynard and Hodge, 1949	NOAEL: None LOAEL: 0.02 ppm uranyl nitrate hexahydrate in food (converted to 2.8 mg uranium/kg/day	1000	1	3E-3 mg/kg/day

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*Conversion Factors: Test compound is 47% uranium by weight (molecular wegiht ratio 238/502). 1 ppm = 0.03 mg/kg/day (assumed rabbit food consumption).

I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

Maynard, E.A. and H.C. Hodge. 1949. Studies of the toxicity of various uranium compounds when fed to experimental animals. In: The Pharmacology and *Toxicology of Uranium Compounds. Nations Nuclear Energy Service. Division* VI, Vol. I, C. Voegtlin, and H.C. Hodge, Eds. McGraw Hill, New York, NY. p. 309-376.

Rabbits, rats and dogs were administered uranium compounds in the diet for 30 days. Studies of rats and dogs were continued for longer periods with serial *sacrifices up to 1 year (rats and dogs) or 2 years (rats only) of exposure.* Rabbits showed greater sensitivity to the toxic effects of uranium. Rabbits (6/group; strain and sex not reported) were fed dietary levels of uranyl nitrate hexahydrate of 0, 0.02, 0.1, or 0.5% for 30 days (equivalent to doses of 2.8, 14, and 71 mg U/kg/day). Animals were examined daily, body weights *were recorded weekly and kidneys were examined histologically at the* termination of the experiment. Mortality was observed at the two highest doses (6 of 6 fed 71 mg U/kg/day, 4 of 6 fed 14 mg U/kg/day). During the first week of exposure, body weight losses were observed at all doses. After 30 days exposure, body weights of rabbits receiving 2.8 mg U/kg/day were *similar to controls. Renal damage was judged to be moderate at the two lower* doses and moderately severe at the highest dose. Based on this study, the lowest dose tested in rabbits (2.8 mg U/kg/day) was judged to be the LOAEL.

The toxicity of uranium compounds was less severe to rats and dogs, although water soluble uranium compounds (UO_2F_2, $UO_2(NO_3)_2$, UCl_4) were more toxic than *insoluble compounds (Maynard and Hodge, 1949). LOAELs for these compounds* were 39, 120, and 160 mg U/kg/day for rats, and 7.7, 9.5, and 132 mg U/kg/day for dogs, respectively. In most cases, LOAELs could be identified within the first 30 days of exposure.

Uranium is a classical nephrotoxic. The toxicity of this chemical to humans has been of interest since the 1800's when uranium was used as a homeopathic *cure for diabetus mellitus (Hodge, 1973). These early reports demonstrate the* susceptibility of humans to the nephrotoxicity of ingested uranium, but provide inadequate basis for estimating the threshold dose for toxic effects.

Hursh et al. (1969) administered single oral doses of uranyl nitrate (10.8 mg U/ 65 to 170 ug U/kg) to four hospital patients. Urinary levels of uranium *and protein were determined. Urinary protein was not elevated in any of the* patients.

Humans have been exposed to uranium compounds by intravenous injection in controlled experiments on uranium excretion and toxicity (Hursh and Spoor, *1973; Lussenhop et al., 1958). Single doses of 120 ug U/kg and higher* administered to terminal brain tumor patients were associated with elevations in urinary excretion of catalase, albumin and non-protein nitrogen, and casts in the urine (Lussenhop et al., 1958). Hursh and Spoor (1973) describe a study in which seven patients were injected with uranyl nitrate (6.3, 6.3, 16, *30, 42, 55, or 71 ug U/kg). Renal function tests were performed including* urinary catalase, protein, nitrogen, glomerular filtration rate, maximum tubular excretory capacity and urea clearance. Trace changes in urinary catalase were noted in patients receiving 55 or 71 ug U/kg.

Novikov and Yudina (1970) administered female rabbits (6 to 8/group) oral doses of uranyl nitrate of 0, 0.02, 0.2, and 1 mg U/kg/day for 12 months. No differences were noted compared with controls with respect to serum urea, creatinine or chlorides. Further experiments on enzyme levels in tissue homogenates were equivocal; enzyme activities were only expressed relative to the wet weight of the tissue from which the homogenate was prepared.

Limited data are available on the reproductive toxicity of uranium. Maynard

and Hodge (1949) conducted a 2-year study of the reproductive effects of uranium. Administration of dietary levels of uranyl nitrate of 2% (equivalent to a dose of approximately 470 mg U kg/day) resulted in decreased food consumption, and declines in weight gain. Decreases in the number of litters born, litter size, were consistent with the decline in nutritional status of the animals.

In a second study by Maynard and Hodge (1949), rats (50/sex) were exposed to dietary levels of uranyl nitrate of 2% (about 460 mg/kg) for one day. Males and females were then paired, over a period of 7 months. Declines in total number of pups born (1959 vs. 1725; 12% decrease) and litter size (8.6 vs. 7.6; 7% decrease) were observed with treatment, but the actual number of litter bearing females increased from 43/50 to 44/50 with treatment.

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- The UF of 1000 reflects 10 for both intraspecies and interspecies variability to the toxicity of the chemical in lieu of specific data, and 10 for use with a LOAEL from an animal study. The uncertainty factor does not include an extra factor of 10 for less-than-lifetime exposure since experiments of acute/subacute duration have been shown to be adequately sensitive for determining doses which cause chronic nephrotoxicity. Rabbits inhaling uranyl nitrate dust (0.25 mg/cu.m) for 10 days showed similar, nephrotoxic effects (interstitial nephritis, tubular regeneration) compared with rabbits exposed to these levels for 6.5 months (Stokinger et al., 1949). Similarly, rats and dogs ingesting uranium compounds displayed similar NOAELs/LOAELs after 30 days exposure compared with exposures of 1 or 2 years (Maynard and Hodge, 1949).

MF -- None

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

Pharmacokinetic models were considered in developing the RfD. Although parameters for absorption, distribution, and accumulation in the kidney are uncertain, reasonable risks can be estimated for these parameters. However, data are inadequate for determining a threshold for uranium levels in the kidney which cause nephrotoxicity and it is questionable whether total uranium levels in the kidney are a good measure of the potential for toxicity. Because of these uncertainties, modeling approaches were not used to determine the RfD.

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study -- Medium
Data Base -- Medium
RfD -- Medium

The critical study is well designed, but used a small number of experimental

animals; it rates medium confidence. The data base is given a medium level of confidence since there are adequate studies on the effects of *U* in various species. Medium confidence in the RfD follows.

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

Source Document -- U.S. EPA, 1985

Other EPA Documentation -- None

Agency Work Group Review -- 01/19/1989

Verification Date -- 01/19/1989

___I.A.7. EPA CONTACTS (ORAL RfD)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) *or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).*

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Uranium, soluble salts
CASRN --

Not available at this time.

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Uranium, soluble salts
CASRN --

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

_VI. BIBLIOGRAPHY

Substance Name -- Uranium, soluble salts
CASRN --
Last Revised -- 10/01/1989

__VI.A. ORAL RfD REFERENCES

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__VI.B. INHALATION RfD REFERENCES

None

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

None

_VII. REVISION HISTORY

Substance Name -- Uranium, soluble salts
CASRN --

Date	Section	Description
10/01/1989	I.A.	Oral RfD summary on-line
10/01/1989	VI.	Bibliography on-line
01/01/1992	IV.	Regulatory Action section on-line

VIII. SYNONYMS

Substance Name -- Uranium, soluble salts
CASRN --
Last Revised -- 10/01/1989

Uranium (soluble salts)

Last updated: 5 May 1998
URL: http://www.epa.gov/iris/subst/0421.htm