AREVA

March 20, 2007
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U. S. Nuclear Regulatory Commission
Director, Office of Nuclear Material
Safety and Safeguards
Attn: Document Control Desk
Washington, D.C. 20555

Gentlemen:

Subject: Revised Response to Request For Additional Information For AREVA NP Inc., Richland Site-wide Integrated Safety Analysis Summary Review (TAC L31856)

On March 2, 2007, AREVA NP (AREVA) provided the NRC with an updated response to the Request for Additional Information (RAI) from the NRC relative to the Integrated Safety Analysis (ISA) Summary for the Richland facility. In this updated response, AREVA committed to provide additional information to support the response to question Ch-29 dealing with intakes of soluble U.

The attachment to this letter provides additional information regarding AREVA's basis for its conservative value. We appreciate your continued consideration in the matter.

Please contact me on 509-375-8409 if you have questions or need additional assistance in support of this response.

Very truly yours,

R. E. Link, Manager
Environmental, Health, Safety & Licensing

/mah

Enclosures

cc: Mr. Merritt Baker, USNRC
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March 14, 2007

Richard K. Burklin, CHP
Areva
2101 Horn Rapids Road
Richland, WA 99354

Dear Rich,

This letter will serve as as an interim progress report, as it were, regarding my independent research into the toxicity of uranium as well as an expansion of the report previously sent you. Acute toxicity is, of course, a high consequence event, and results in the death of the worker if untreated within a short period of time after exposure, usually taken to be 30 days. As mentioned to you previously, before the discovery of insulin, uranium, orally administered, was used to treat diabetes mellitus, and there is a significant body of medical literature dealing with this topic. Typical doses ran to several grams of uranium administered daily, for periods of several months. We have now obtained several papers published in the medical literature prior to 1918 describing the clinical results of treatment of diabetics with soluble uranium *per os*. Although the total intake of uranium by some of the patients so treated amounted to several grams daily, there were no deaths in these patients nor were toxic effects, including indication of significant kidney toxicity, observed. Indeed, in describing his own observations, Reynold Webb Wilcox, President of the American College of Physicians, wrote (*Medical Record* 92(9):361-364, September 1, 1917):

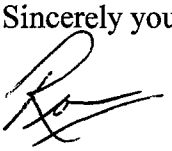
> "In all instances in which I have employed uranium nitrate I have never noted any untoward gastric or intestinal symptoms nor any signs of blood or renal disturbances; careful observation has been especially directed toward early detection of the latter"

Review of these papers plus the report of a case from the United Kingdom of an individual who ingested a single dose of 8.4 g of uranium (as acetate – 15 g of uranium acetate were ingested) and data from animal toxicity studies suggests that the lethal dose of orally ingested soluble uranium is at least several grams, and this amount corresponds to an inhalation intake of soluble uranium of several hundred milligrams, and quite possibly as much as several grams, assuming Class F uranium and a particle size distribution of 5 μm AMAD with $\sigma = 2.5$ μm. This contrasts sharply with the LD_{50} of 230 mg put forth in Table 2 of NUREG-1391.

With respect to kidney toxicity, note that following an acute intake of soluble uranium, a large fraction of the uranium is excreted via the kidney quite rapidly; most biokinetic models indicate that about 70% of the intake of soluble uranium is excreted within the first 24 hours after intake. A much smaller fraction is actually taken up by the kidney, and is only slowly removed and hence retained there for a long period of time. Minor, transitory and completely reversible kidney effects have been noted in persons with high acute accidental inhalation intakes of

uranium, but long term renal effects have not been observed in humans following acute exposures, or long term chronic exposure via drinking water. A reasonable comparison can be made of the potential peak kidney burden from the chronic oral ingestion typical of treatment for diabetes described above with intake via inhalation. By determining the peak kidney burden from the oral intakes, an equivalent inhalation intake, that is, one which theoretically produces the same peak kidney burden as the oral intakes, can be calculated using available standard biokinetic models. This was done for 10 cases treated with uranium; the calculations indicate that to produce a theoretical peak kidney concentration from inhalation equivalent to that in the treated individuals would require an inhalation intake averaging about 1.5 g and ranging from a few hundred mg to more than 3 g. It is clear that the intakes experienced by these patients are many fold greater than the acute intake level of 40 mg for a 70 kg person (Reference Man) cited in Table 2 of NUREG-1391 as the threshold for permanent renal damage. Moreover, they are consistent with data from two individuals estimated to have incurred acute inhalation intakes of 80-100 mg with no observed kidney pathology 38 years post exposure, and with three individuals with chronic inhalation intakes ranging from a tens to hundreds of mg of U who were found to have no kidney pathology at autopsy. Thus it seems safe to say that the 40 mg value put forth in NUREG-1391 as the threshold for permanent renal change is certainly quite conservative and bears further evaluation with an eye towards its possible upward revision.

Sincerely yours,



Ronald L. Kathren, CHP, DEE

Paper	Calculated Acute Peak Kidney Burden from Ingestion (mg)	Calculated Acute Inhalation Intake Required for Equivalent Kidney Peak Burden (mg)
Bond Case 1	2.5E+01	7.5E+02
Bond Case 9	1.2E+02	3.8E+03
Duncan Case 1	2.4E+01	7.4E+02
Duncan Case 2*	3.3E+01	1.0E+03
Duncan Case 3	6.5E+01	2.0E+03
Duncan Case 4	5.1E+01	1.6E+03
Duncan Case 5	3.2E+01	9.9E+02
West (1895) Case 1	5.2E+01	1.6E+03
West (1895) Case 3	3.9E+01	1.2E+03
West (1896) Case 3	2.4E+01	7.3E+02

Autopsies were performed on the cases below. The histolopathological findings were comparable to those seen in terminal patients without exposure to uranium.

	Calculated Acute Peak Kidney Burden from Injection (mg)	Calculated Acute Inhalation Intake Required for Equivalent Kidney Peak Burden (mg)
Hursh and Spoor Case 6	3.5E+00	1.1E+02
Hursh and Spoor Case 7	2.9E+00	9.7E+01
Hursh and Spoor Case 8	3.2E+00	9.0E+01

*Differences between chart and verbage.

References:

Bond, C.H.: Remarks upon the value of uranium nitrate in the control of glycosuria. Practitioner, 257-264, Sept. (1898)

Duncan, E.: The treatment of diabetes mellitus by nitrate of uranium. Brit. Med. J. (1897), II 1044-1047

West, S.: The treatment of diabetes mellitus by nitrate of uranium. Brit. Med. J II 467-472 (1895)

West, S.: Further observations on the treatment of diabetes mellitus by nitrate of uranium. Brit. Med. J (1896) II 729-730 (1896)

Hursh, J. B. and N. H. Spoor. Data on Man. Chapter 4 in *Uranium Plutonium Transplutonic Elements* (H. C. Hodge, J. N. Stannard and J. B. Hursh, Eds). Handbook of Experimental Pharmacology XXXVI. New York: Springer-Verlag, 1973, pp. 197-239.

West, S.: The treatment of diabetes mellitus by nitrate of uranium. Brit. Med. J (1895) II 467-472

West, S.: Further observations on the treatment of diabetes mellitus by nitrate of uranium. Brit. Med. J (1896) II 729-730 (1896)