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DIVISION OF
NUCLEAR MEDICINE

10 June 1997

D. Blair Spitzberg, Ph.D.
United States Nuclear Regulatory Commission
Region IV
611 Ryan Plaza Dr., Suite 400
Arlington, TX 76011-8064

Re: Report of Medical Consultant Regarding I-131 Administration to a Pregnant Patient
(License 05-26854-01; Docket 030-29534)

Dear Dr. Spitzberg:

I am responding to the letter dated 23 May 1997 from E. Merschoff, Regional Administrator, requesting that I provide medical consultation services with respect to the above-name incident. The sources of information that I used in preparing this report include a copy of the Preliminary Notification of Event or Unusual Occurrence (PNO-IV-97-028) supplied to me by Region IV, as well as records provided to me by the licensee (Evans Army Community Hospital). Specifically, the licensee provided me with a copy of a Memorandum for Record dated 16 May 1997 regarding this incident, the Dose Tracking Log dated 3 April 1997 for this I-131 administration, the Procedure Worksheet dated 3 April 1997 for the I-131 therapy, the Patient Consent Form dated 3 April 1997, the patient's laboratory test records, and the radiologic examination report dated 7 April 1997 describing the I-131 therapy. I conducted two telephone interviews with the authorized user physician, Royce K. Solano, M.D..

Based on the information available to me, I offer the following observations and conclusions.

The Patient: The patient is a 26-year-old woman with hyperthyroidism referred to the licensee's facility for treatment with I-131 sodium iodide. According to Dr. Solano's records, this patient was known to have had hyperthyroidism due to diffuse toxic goiter (Grave's disease) at least since October 1996. Subsequent laboratory studies confirm continuing hyperthyroidism. The laboratory studies obtained on 18 March 1997 (approximately 2.5 weeks before I-131 therapy) were as follows: serum free thyroxine 2.71 ng/mL (normal range 0.71-1.85 ng/mL) and serum thyrotropin (TSH) < 0.04 μIU/mL (normal range 0.47-5.01 μIU/mL). The radioactive iodine uptake measured on 18 February 1997 was 75% at 6 hours and 52% at 24 hours. Physical examination demonstrated a moderately enlarged thyroid gland (estimated at 50 grams) without palpable nodules. The Procedure Worksheet for I-131 therapy indicated that the patient had been questioned regarding pregnancy and breast feeding and denied both. The pregnancy test (quantitative beta-HCG) was obtained on 1 April 1997 and was misinterpreted as a negative result by Dr. Solano (hence, the basis for this incident). Specifically, Dr. Solano appears to have misread the normal test value (< 2 μIU/mL) as the actual test result in this patient, when the reported test result actually was 4045 μIU/mL, a clearly positive result. At the time of I-131 administration, the patient was taking no medications expected to alter the biodistribution or pharmacokinetics of I-131. There were no complicating medical problems.

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The Incident: On 3 April 1997, the patient received a 10.0-mCi capsule of I-131 sodium iodide orally as treatment for her hyperthyroidism. The patient subsequently did well, until early in May of 1997 when she contacted her primary care physician because of nausea. The primary care physician reportedly examined the patient and ordered laboratory tests, including a pregnancy test. The pregnancy test was positive. The primary care physician notified Dr. Solano that the patient was pregnant on 14 May 1997. The primary care physician estimated the date of conception to be 20 March 1997 (2 weeks prior to I-131 administration). Dr. Solano contacted the Radiation Internal Dose Information Center (RIDIC) at Oak Ridge, TN on 14 May 1997. The radiation exposure to the embryo was estimated to be 1.3 rem based on a radioactive iodine uptake of 76% (see below). On 15 May 1997, the patient underwent pelvic ultrasonography; the results of this study reportedly were normal. The Nuclear Regulatory Commission was notified of this incident on 16 May 1997.

Radiation Dose: The radiation dose to the patient is not relevant, since the radiation exposure she received was consequent to an appropriate prescribed dosage of I-131 for her medical condition (and her presumed non-pregnant state). The radiation dose to the embryo can be estimated from the thyroid uptake values by the method of Stabin et al. ("Radiation dosimetry for the adult female and fetus from iodine-131 administration in hyperthyroidism. *J Nucl Med* 1991; 32:808-813). With this method, a short biologic half-time for thyroidal uptake can be assumed when the 24-hour uptake value is less than an earlier value, ads was the case in this patient. Dr. Solano's report of the I-131 treatment quotes a 6-hour radioactive iodine uptake on 18 February 1997 of 75% and a 24-hour uptake of 52%. Under these circumstances, the uterine (and fetal) radiation dose with a 75% maximum uptake is estimated by interpolation to be approximately 0.136 rem/mCi. The only radiation exposure estimate of relevance in this case is the total embryo dose given above. Because the fetal thyroid gland does not begin to accumulate iodide ion until approximately 10 weeks, no increased thyroid radiation dose would be expected in this case.

Medical Consequences of the I-131 Administration: It is unlikely that a radiation exposure of 1.36 rem to an embryo of approximately 14 days post-conception age at the beginning of the exposure will result in any clinically detectable effect. Since most of the radiation exposure to the embryo derives from excreted I-131 in the urinary bladder, most of the exposure will have occurred in the first 24-48 hours after I-131 administration. Based on *NCRP Commentary No. 9. Considerations Regarding the Unintended Radiation Exposure of the Embryo, Fetus or Nursing Child* (Bethesda, MD:NCRP; 1994), radiation exposure in this case occurred near the end of the period of gestation when lethality with resorption of the embryo would be most likely effect and near the beginning of the period when gross malformations would be the most likely effect. However, these deterministic effects generally occur above a threshold of 100 rem, although some evidence suggest thresholds for malformations and growth retardation in the range of 10-20 rem. The exposure in this case is well below these thresholds. Moreover, the modulating influence of a low dose rate, although not known with certainty, is likely to reduce the risk even further.

The stochastic effect of concern is carcinogenesis. Although there is moderate uncertainty in the data used for cancer risk estimation as the result of *in utero* radiation exposure, a reasonable estimate of the risk during the first 10-14 years of life for leukemia and other childhood cancers following *in utero* radiation exposure is approximately 0.05% per rem. Accordingly, in this case with an upper-limit fetal effective dose of 1.36 rem, an excess risk of about 0.07% is estimated. For comparative purposes, the natural risk of childhood cancers is about 0.1%. Thus, the risk is increased by about 70%. However, stated another way the

probability that the exposed embryo will **NOT** develop a radiation-induced childhood cancer is >99.9%. It is unknown whether this risk estimate should be reduced because of the low dose rate associated with this exposure from I-131.

In my opinion, the impact of the I-131 administration on the health of this patient's embryo/fetus is very low.

Medical Follow-up and Care Required: Other than the ordinary care required for continuing treatment and follow-up of the patient's hyperthyroidism, as well as routine prenatal care of a pregnant hyperthyroid patient and routine pediatric care of this infant following delivery, no specific medical care or follow-up is warranted as a result of this inadvertent administration of I-131 during pregnancy.

Medical Information Provided to the NRC by the Licensee: Records supplied to me by the licensee indicate that the patient and her primary care physician have been notified of this inadvertent radiation exposure to the embryo/fetus. The information provided to these individuals concerning the low risk of adverse consequences from this radiation exposure is consistent with my opinions above.

Department of Energy Office of Epidemiology and Health Surveillance Long-Term Medical Study Program: In my opinion, the nature and magnitude of the radiation exposure to this patient's embryo/fetus do not warrant enrolling the infant after delivery in the DOE Long-Term Medical Study Program.

Please let me know if you need additional information.

Sincerely yours,

Barry A Siegel MD

Barry A. Siegel, M.D.
Professor of Radiology and Medicine
Director, Division of Nuclear Medicine

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