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April 23, 2003

Ms. Cassandra F. Frazier
US Nuclear Regulatory Commission
Region III
801 Warrenville Road
Lisle, IL 60532-4351

Dear Ms. Frazier:

I have reviewed the medical event which took place 3/28/03 when 421 mCi of sodium iodide-iodine-131 was given to a 9 year old patient.

Causes:

1. The technologist who initially ordered the iodine-131 was apparently unaware that there was a difference between iodine-131 and iodine-123.
2. This technologist further did not recognize that the dose of iodine-131 for diagnostic purposes is 1% of that dose which was ordered.
3. When this arrived, it was presumably placed in a dose calibrator. The Quality Management Program of the hospital would presumably require that the technologist and an authorized user would both note that any dose of iodine-131 in excess of 30 uCi would need a written order. There is no evidence that there was a written order from an authorized user or that one was sought.
4. The second technologist involved did not employ the Quality Management Program of the hospital (if there is one), requiring a written order, etc., before administering iodine-131.
5. The radiologist who was presumably the authorized user should have immediately looked for a written order for iodine-131, rather than assuming that someone had made a "computer data entry error".

Dosimetry:

The appropriate model, I believe, that employed by the Radiation Internal Dose Information Center in Oak Ridge Tennessee in the document entitled "Radiation Dose Estimates to Adults and Children From Various Radiopharmaceuticals", updated 4/30/96 was used for dosimetry. As noted in the cover letter from Robert T. Anchor, Jr., the thyroid dose estimate is 1370 rem and the estimated effective dose equivalent 42 rem.

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Deterministic Effects:

No acute radiation effects would be anticipated to any organ, since no organ (except the thyroid) received more than 1.0 rad from this dosage of iodine-131, according to the RIDIC data noted above. The 1370 rem dose will not cause radiation thyroiditis.

Stochastic Effects:

Predicting the chronic effects on the thyroid gland is difficult because there are very few data on the administration of iodine-131 to 9-year old patients who do not have an overactive thyroid or where there is not a mixture of iodine radioisotopes.

There are considerable data on the risks of external beam radiation in carcinogenesis as when this has been employed for epilation of ringworm, or treatment of other benign or malignant conditions. However iodine-131, with a low dose rate, would be expected to have a biological effectiveness of 0.2-0.5 of that of external beam therapy. This has been found in several reviews of iodine-131 effects, as for example Maxon, et. al, American Journal of Medicine, 1977; 63: 967-978.

There are many descriptions of thyroid cancer occurring after oral iodine-131 therapy for thyrotoxicosis, but analyses of these have not shown an increase beyond what one would expect in the general population. In addition, Graves' disease appears to be associated with a mildly increase risk of thyroid cancer, so that these data would not be applicable to this previously euthyroid patient.

The thyroid cancer resulting from the Chernobyl disaster has been well publicized, but these malignancies were related not only to iodine-131 but to short-lived iodines such as iodine-132 and iodine-133 which have higher dose rates, so that one cannot easily extrapolate to our patient. The appearance of thousands of carcinomas in children under 10, most striking in children who were under 4 at the time of the exposure, cannot be dismissed however. In thyroid doses reconstructed for 11 of several thousand children with thyroid carcinoma, the dose ranged between 30 and 1000 cGy, while this current patient had a thyroid dose which was calculated at 1302 cGy (rem) (Nikiforov, Y.E., et al. Thyroid Today 1998; 21: 1-11).

Thyroid carcinoma was also increased in Marshall Islanders as a late response to bomb testing fall-out. The risk for thyroid nodules (about 10% of which proved to be cancer) was 11.0 excess cases per cGy per year per 10^6 patients. However there was again a mixture of radioiodines involved here, with iodine-131, iodine-132, iodine-133 and iodine-135 (Hamilton, T.E. JAMA 1987; 258: 629). Nevertheless the risk of nodules and carcinoma simply cannot be dismissed. In the review of available data by Maxon, et. al. noted above, the authors suggest "that a realistic threshold for the induction of hypothyroidism by exposure to radioiodine-131 would be 20 rem (cGy). At this time there are no data in human subjects to refute this hypothesis". There are simply insufficient data in juveniles to be reassured that a radiation dose in excess of 1300 rem to

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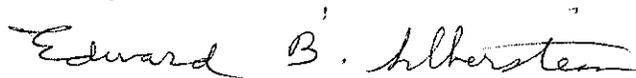
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the thyroid would have no long term consequences, given the increase in radiosensitivity of the thyroid glands of children.

Medical Recommendations:

1. The NRC will undoubtedly supervise the QM program of this hospital to be sure that there is compliance, since this appears to have been a "root cause" of the patient receiving this inappropriate dose of iodine-131.
2. I am not able to provide reassurance to the patient and her family that there are no long-term effects from this radiation and disagree with the note of Linda White, President of Deaconess Hospital, to Mr. Robert Hayes of the NRC dated April 14, 2003.
3. Hypothyroidism is possible and may occur after many years, so that an annual serum TSH should be obtained for the foreseeable future, with a baseline obtained now.
4. The appearance of thyroid nodules or, less likely, thyroid carcinoma cannot be excluded in this patient because of the radiation dose received of by thyroid gland and the known radiosensitivity of children's thyroid glands. The patient should be followed with neck ultrasound. Similarly, any neck lymphadenopathy that does not disappear within 4 weeks in this child should be evaluated very vigorously.

Cordially,



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