UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
AIR AND RADIATION

Ms. Ann M. Witt
Acting Associate Commissioner for Policy
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

Dear Ms. Witt:

The Environmental Protection Agency (EPA) appreciates the opportunity to provide comments on the Food and Drug Administration's (FDA) proposed guidance "Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies." [Docket No. 00D-1681] The EPA has carefully reviewed the proposed guidance and has enclosed five comments. If you have any questions, please feel free to call Mr. Craig Conklin, Director of the Center for Radiological Emergency Preparedness, Prevention, and Response at (202) 564-9222.

Again, thank you for the opportunity to comment on this important guidance.

Sincerely,

Frank Marcinowski, Acting Director
Radiation Protection Division

Enclosure

00D-1681 C10

EPA's Comments on ""Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies"

1. Page 4, Section III. B. *Thyroid Cancers in the Aftermath of Chernobyl* - Because the FDA is recommending that KI not be utilized unless the projected dose is 5 cGy or greater, EPA recommends the incorporation of a data table that summarizes the "best dose-response information from Chernobyl" from the three referenced sources so that the basis for this recommendation can be more fully understood.

2. Page 5, Section IV. B. *KI use in radiation emergencies: treatment recommendations* - The first paragraph states that KI is not a recommended protective action for adults over 40 unless the projected dose to the thyroid is $\geq$ 500 cGy. This values is 100 times the thyroid dose for a pregnant/lactating women and persons 18 years of age and younger, for whom KI is strongly urged and 50 times the value for adults aged 18-40. EPA recommends that the risks associated with administration to adults over 40 be more fully characterized in order to support this recommendation.

3. Page 4, Section III. B. *Thyroid Cancers in the Aftermath of Chernobyl* - The FDA draft guidance puts the rate of adverse reaction at 0.37% for a minor increase in thyroid stimulating hormone, 2% for gastrointestinal distress in children and 1% for a minor rash in children and adults, with only 2 allergic reactions reported in a population of about 17.5 million people who received KI. All the non-allergic reactions were deemed clinically insignificant. The life-threatening reaction rate appears to be something around 2 in 20 million, or about ten to the minus seven, well below the acceptable level of one in ten- to a hundred thousand. By placing the recommended dose for intervention at a dose to the thyroid comfortably below the range where excessive thyroid cancers were detected in the population at Chernobyl, it appears the FDA is not using a linear assumption for radiation risk. The proposed guidance needs to address this apparent discrepancy.

4. The proposed guidance still seems to downplay some aspects of the risks associated with the administration of KI. For example, the extent of possible complicating conditions is not noted; e.g. patients with allergic conditions, with underlying thyroid disease, receiving lithium therapy; people with chronic iodine deficiency, with iodine induced goiter, with a family history of goiter or thyroiditis. (1,2) The American Thyroid Association still does not know of any data on the number or proportion of the US population with sensitivity to iodine. In addition, there is a lack of data on how much iodine is required to sensitize a person to iodine, or if multiple exposures are required, and how many persons in a population could be sensitized by thyroid blocking doses of KI. Finally, while noting that 12 of 3214 neonates in Poland showed a transient response to a single 15 mg dose of KI, they do not note that this was in a report from a single

endocrine clinic in the City of LODZ. The EPA recommends that the FDA initiate studies to determine the baseline rate of iodine sensitivity in the general US population so that decision makers have a better idea of how many people may be put at risk should they decide to administer KI as a blocking agent.

(1) Elliot Sternthal, et al. A Suppression of Thyroid Radioiodine Uptake by Various Doses of Stable Iodide in New England Journal of Medicine, 303: 1083-1088 (1980).

(2) Howard Backer and Joe Hollowell. Use of Iodine for Water Disinfection: Iodine Toxicity and Maximum Recommended Dose in Environmental Health Perspectives. 108: 679-684 (2000).

5. Based upon the information generated in the response to the Chernobyl accident, there is no question that the benefits of KI administration to reduce the risk of thyroid cancer in children outweighs the risks associated with the administration of the KI. There is also a potential for doses as low as 1 cGy to cause thyroid cancer, it seems that the conservative action to take would be to administer KI when the projected dose is equal to or greater than 1 cGy rather than 5 cGy. The EPA recommends that the FDA needs to provide a stronger basis for deviating from the World Health Organization's recommendation of administering KI when the projected dose is equal to or great than 1 cGy.