Peter G. Crane / 6545 27th Avenue, NW / Seattle, WA 98117-5902 / 206- 783-8485 / cranepbko@yahoo.com

February 11,2001

Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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Re: Docket No. OOD-168 1, Draft Guidance on Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies

To the Dockets Management Branch:

I. Summary

The draft guidance&r potassium iodide (KI) newly issued by the Food and Drug Administration is a credit to the FDA and a major service to the American people, state and local governments, and the' other agencies of the federal community. Scientifically objective, well-reasoned, lucid; and concise, it answers the outstanding questions on KI, and in partidular provides decisionmakers at the state and local level with the information they need to determine whether stockpiling makes sense for them. It also rebuts definitively the mendacious propaganda, masquerading as science, with which the NRC technical staff, in the 1998 Congel-Mohseni report ("Draft NUREG-1633"), purported to offer a technical assessment of KI. The FDA draft guidance requires no revision and should be adopted in final form. Its issuance reinforces the need for the NRC to refrain from meddling in issues of drug safety and effectiveness, matters on which it is as little qualified to speak as is FDA on issues of nuclear'power plant safety.

II. The Draft Guidance

The draft guidance, among other things:

- reaffirms and strengthens the FDA's 1982 "safe and effective" finding on KI.
- makes the point that the incidence of childhood thyroid cancer in Chernobyl-affected areas has risen as much as 100-fold; that the "dramatic increase in thyroid cancer among exposed children," with a "relatively short latency,"' is produced even by "relatively small doses of radioiodine."
- stresses the Polish experience with KI, which shows the drug's "safety and tolerability."
- makes the point that the benefits of KI treatment for neonates to reduce the risk of thyroid cancer outweigh the risk of side effects, but also provides guidance for minimizing risks of such side effects.
- by lowering to 5 cGy the intervention level for KI in children, provides guidance reflective of the Chernobyl experience.
- stresses the time-critical nature of KI administration — an implicit argument for having supplies on hand, rather than at some distant location.
- emphasizes that KI is not intended to be used as the sole means of radiation protection, but rather "as an adjunct to evacuation (itself not always feasible), sheltering, and control of foodstuffs."
- complements and reinforces the recent decision of the Nuclear Regulatory Commission, which (overriding a contrary recommendation of the NRC technical staff) published a final regulation requiring states to consider KI as part of nuclear emergency planning.

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- makes apparent the wisdom of the recommendation, adopted in 1996 by the Federal Radiation Protection Coordinating Committee, that the federal government should supply KI to any state wishing to establish a stockpile. (The NRC, as part of its recent decision, endorsed this approach and undertook to bear at least the initial cost.)

A question raised by some commenters is whether the 5cGy intervention level is sufficiently conservative, and whether the 1 cGy level advocated by Dr. Keith Baverstock of the World Health Organization would be more desirable. In my view, the FDA has acted wisely in following the path it has chosen, given the eminence of those whose views it reflects, including Drs. Jacob Robbins and Jan Wolff of NIH, Dr. David Becker of the New York/Cornell Medical Center, and the American Thyroid Association. If at some point in the future, evidence points more strongly than it does today to a lower intervention threshold, FDA can and no doubt will act accordingly. For the present, however, to move immediately to a 1 cGy level, solely on the basis of the WHO report, would raise questions as to whether FDA was acting precipitately, and probably serve to impede rather than promote the widespread adoption of KI stockpiling in the United States. Accordingly, I believe that the draft guidance should be made final without any alteration in the 5cGy standard.

III. **The Draft Guidance in Relation to Draft NUREG-1633**

The FDA draft guidance presents the strongest possible contrast with the Congel-Mohseni report of 1998 ("Draft NUREG-1633"). It is worth discussing the NRC report in some detail, because the presence of the draft guidance from FDA raises the question whether there is any continuing need for NUREG-1633, at least in anything like the form in which it was originally issued.

The Congel-Mohseni report purported to be a technical analysis by the NRC staff of the safety and effectiveness of KI. In reality, it appears to have been an attempt to negate the FDA's 1982 "safe and effective" finding by creating a rival document, seemingly authoritative, that would serve to persuade NRC Commissioners and state governments that KI was dangerous to health and that stockpiling the drug was therefore undesirable.

The single best measure of the level of integrity of the Congel-Mohseni report was its handling of the FDA's 1982 "safe and effective" finding. One would naturally have expected this finding to be the starting point of their analysis, given that the FDA and not the technical staff of the Nuclear Regulatory Commission is the national authority on the safety and effectiveness of drugs. Instead, the authors dealt with this troublesome fact by never mentioning it all all. Their failure to refer to the FDA finding cannot have been for lack of space, as the report was 40 pages long. The omission speaks volumes. It is precisely as though FDA were to issue a lengthy report decrying the supposedly perilous condition of the Seabrook nuclear plant without mentioning that there was another agency, the Nuclear Regulatory Commission, that regulated such plants, and that Seabrook had met the NRC's "reasonable assurance of safety" test.

Another uncomfortable fact for the report's authors was the Polish experience with KI during Chernobyl. Their response was to express doubt about the veracity of the Polish experts. "To the extent we believe the Polish data," the authors wrote at one point, without explaining what reason there was to doubt that

data. This slur on their betters was one of the most deplorable aspects of the report. I am happy to say that a more senior NRC staff manager subsequently invited the leading Polish expert on KI to come to the NRC to discuss his use of KI during the Chernobyl accident — an implicit apology for his subordinates' sorry conduct.

The authors of the NRC report appear to have found their lack of expertise in medicine and pharmacology to be no barrier to passing judgment in these areas. Bypassing the directly relevant journal literature, they relied instead on an outdated copy of the *Physician's Desk Reference* (*PDR*), which was cited selectively and out of context. For example, ominous warnings in the report on the side effects of KI turned out to be quotations not from the *PDR*'s description of over-the-counter KI pills for thyroid protection, but from the description of a different, prescription-only drug, used for certain pulmonary diseases, that contains KI in a far more concentrated form. The ordinary reader would have had no reason to suspect that the warnings did not pertain to the drug that was the subject of NUREG-1633. One of the quoted warnings, on the hazard to children with cystic fibrosis, appears either to have been made up out of whole cloth or lifted from the description of some unrelated drug.

What is most remarkable is that the NRC technical staff seems to have imagined that this perverse travesty of good science would pass muster, and that its bias and distortions would go unnoticed. (It is particularly revealing of the authors' disrespect for the intelligence of the NRC Commissioners.) In reality, however, the one redeeming feature of the Congel-Mohseni report was the clumsiness of its execution. The knowledgeable reader was no more likely to be taken in than a shopkeeper presented with an eight-dollar bill.

Consider, for example, the September 28, 1998, comments on the report from Dr. Karim Rimawi, the Director of the Bureau of Environmental Radiation Protection in the New York State Department of Health, who wrote that after the state's Radiological Health Advisory Committee had "found no health related reasons why KI could not be used" for iodine prophylaxis in an emergency, the Department had begun a review to determine if there were logistical or legal reasons not to make potassium iodide an option in radiological emergencies. Dr. Rimawi, who also provided nine pages of detailed criticisms of the report, continued:

> The department had looked forward to NRC's report in the hope that it would assist us in the review. Unfortunately, we find the document to have been prepared to justify a position advocating against the use of KI for public protection, rather than as an objective review of the relevant information. This bias raises doubt as to the value of the document.

Tendentious, unobjective, biased, and of dubious value: quite extraordinarily scathing comments from a state official on a federal agency's efforts, but then the Congel-Mohseni report was hardly an ordinary piece of work. Ohio state officials also filed highly critical comments.

Fortunately, the NRC Commissioners took note of the criticisms, quickly recognized the deficiencies in NUREG-1633, and ordered the document withdrawn from circulation and taken off the NRC website. On October 12, 1998, the trade publication *Inside N. R. C.* published an article entitled "COMMISSION

APPROVES KI NOTICE TO FRPCC, ORDERS DRAFT NUREG WITHDRAWN." It quoted Commissioner Edward McGaffigan as follows:

> "As one staffer has pointed out to me," McGaffigan said, "it [NUREG-1633] was never intended to be supportive of the policy the Commission established in its June 26 SRM, but was instead a justification for the policy (not granting the revised petition for rulemaking) which the staff had advocated and the commission rejected. . . . I made the mistake of thinking no harm could come from just putting a document out for public comment. I was wrong."

Since 1998, the NRC staff has supposedly been revising the document, with the help of a "Core Group" of about 12 persons. Apart from giving a boost to the economy of Arizona — the then leader of the Core Group, Mr. Mohseni, took the group to Tempe, Arizona, for a week in February 1999 — it is hard to see what this effort has accomplished, for all the time and money that has been expended. So far, nothing has been issued.

In one sense, however, this may be fortunate. The FDA guidance has so thoroughly and definitively illuminated the relevant issues on KI that no beneficial purpose would be served by having the NRC cover the same ground in its revision of NUREG-1633. Assuming that NUREG-1633 needs to be reissued at all, it should incorporate by reference the FDA draft guidance, making clear that NRC does not and will not second-guess FDA's findings on the safety and effectiveness of drugs. (It might usefully discuss, however, such issues as the logistics of KI stockpiling and distribution.)

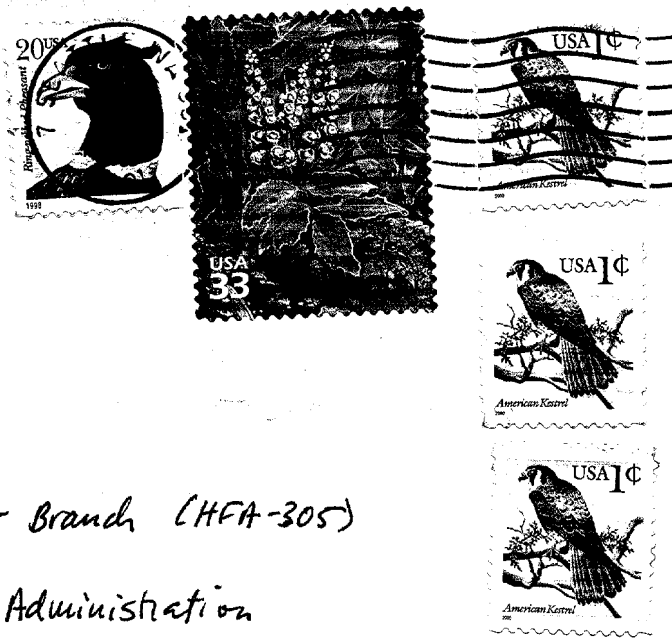
It does not serve the interests of the Government as a whole, or of the FDA, or the NRC, or anyone else, to have two separate federal agencies — one possessing both jurisdiction and expertise, the other possessing neither — offering what purports to be authoritative guidance on the safety and efficacy of a pharmaceutical. The potential for confusion and mischief is too great to allow any further poaching by the NRC staff on FDA's territory. It is therefore essential for the NRC to recognize the limits of its authority, and to curb any signs of rogue behavior on the part of its staff. At the same time, it is incumbent on FDA to maintain its vigilance against interference and intrusion by sister agencies.

Sincerely,

Peter G. Crane

Peter G. Crane

P. Crane
6545 27th Ave. N.W.
Seattle, WA 98117



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