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James W. Neton, PhD, CHP
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Dear Dr. Neton:

Enclosed is my review of the "NIOSH-Interactive RadioEpidemiological Program (ver. 4.0b) Technical Documentation" which you requested. I hope they are helpful in your review process.

The time required for this review was two days. Please address all correspondence to the address given on the letterhead.

Sincerely,

Roy E. Shore

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Comments on, "NIOSH-Interactive RadioEpidemiological Program (ver. 4.0b) Technical Documentation" Dated October 18, 2001

by Roy E. Shore
New York University School of Medicine

The most serious problem with the NIOSH approach – like the NIH/CDC approach – is that cancers with essentially no evidence that they are radiation-inducible, but which have wide confidence intervals because the data concerning them are sparse, may have 99th percentile probabilities (per given dose) that are higher than those for some well-documented radiation-induced cancers. A rational strategy needs to be developed that does not create this nonsensical result (for example, more rational approaches might be grouping of sites as suggested by the National Academy of Sciences Committee, or use of the central estimate of effect rather than the 99th percentile, but with a pay-line at, say, 10% or 20% probability.)

P. 3, last 4 lines: The documentation should stand largely on its own. In this case, potentially major factors in the risk assessment (method of modeling cancer risk from the Japanese data, uncertainty distribution for cancer latency, and stochastic distributions for RBE and DDREF) are acknowledged but not explicated. These surely need to be described fully in the Final Draft.

While it is often acknowledged that the RBE for orthovoltage x-rays is greater than unity, I have not heard of a proposed central estimate as great as 2.7. I therefore looked it up in the Kocher D, et al. Draft on Radiation Weighting Factors which accompanied this document. On P. 8, middle paragraph, Kocher proposes the value of 2.6 (there is a discrepancy: the text says 2.6 but Table 1 says 2.7), but gives virtually a "black box" as justification for it. There is no information given as to: 1) which data from NCRP, 1990 were used, 2) what the biological endpoints were included, 3) how relevant those endpoints are to human cancer induction by radiation and a selection of the most relevant endpoints, 4) whether any evaluation of the quality of the studies that went into the estimate was made (and, for instance, only the better quality ones included), or 5) what dose ranges were used in the data from which the RBE estimate was derived. For a point as important as this one, there should be "full disclosure" and a thorough review by knowledgable people. As it is, it cannot be meaningfully evaluated, because no data or rationale is presented.

P. 5, last paragraph, lines 1-2: From what we know from thousands of dose measurements made over the years at fairly short intervals (e.g., daily or weekly doses in the early years of the DOE facilities) the doses were nearly all highly fractionated and/or protracted. It is therefore unrealistic to make the assumption that all the gamma and x-ray doses are acute over the badge measurement time. In addition, the effects of acute doses smaller than about 10-20 cGy are

generally considered to tempered by DDREF, but the discussion does not indicate that that is so in these calculations. Furthermore, assuming that all gamma and x-ray doses are acute, but simultaneously assuming that all neutron doses are chronic (p. 6, line 7) is a conspicuous inconsistency.

Since there are already highly conservative factors built into the calculations of risk (e.g., using the 99th percentile), adding another (unlikely) conservative factor by assuming totally acute doses and thereby eliminating the DDREF for gamma/x-ray seems to be overkill.

P. 10-12: The discussion of skin cancer radiation effect and race/ethnicity seems to throw together a series of obliquely related issues to somhow infer that non-Caucasians will have a greater probability of radiation causation per unit dose than will Caucasians. However, this conclusion is belied by the most direct evidence, namely, that the Japanese atomic bomb study has an excess relative risk coefficient (per unit dose) that is greater than those for European-derived populations (see Table 1 of Shore RE. Radiation-induced skin cancer in humans. Med Pediatr Oncol 36:549-54, 2001). Likewise, the dark-skinned Israeli population had an ERR/Gy that was as large as those for lighter skinned populations. This is compelling evidence that refutes the indirect reasoning that the document tries to use to infer greater radiation causation among non-Caucasians.

(Furthermore, I might mention that the largest series of radiogenic skin cancer cases, namely, the New York tinea capitis study, shows that the risk to sun-exposed skin is as great or greater than that to sun-protected skin, so it is questionable to use the contrary line of reasoning, based on the smaller atomic bomb study, that radiation risk is greater in sun-protected skin.)

P. 15, the equation: A minor point, but the last part of the exponent should be 1.645, not 1.642.

P. 15, 5-6 lines from bottom: No age-specific risk coefficients were provided in the atomic bomb study for squamous cell carcinoma (SCC) because the risk coefficient was in the negative direction. Furthermore, you should check with Charles Land before imputing the basal cell risk coefficient for SCCs. He tells me that a more extensive analysis of the SCC data indicates that it is nearly statistically significant in the <u>negative</u> direction. It therefore seems to be bad science to assign it a substantial positive risk coefficient; rather, it should be dropped.

P. 16, middle paragraph: This seems to be a very selective review of the malignant melanoma literature. I suggest you see ICRP, 1991a (in your references) or Shore, 1990 (Overview of radiation-induced skin cancer in humans. Int J Radiat Biol 57:809-27) and incorporate a more complete review.

P. 17, last paragraph: Since there is virtually no evidence that malignant melanoma is induced by ionizing radiation, except perhaps at extremely high doses (cf. Shore, 2001 in your references), it is inappropriate to assign the basal cell carcinoma risk coefficient to it.

P. 18, paragraph 1, near the end: The conclusion of the Land study regarding interactions between hormonal factors and radiation with respect to breast cancer is that most of the hormonal factors did not interact. Furthermore, you should look at the other papers that have evaluated this and have found mostly negative results (namely, Boice J, Stone B. Interaction between radiation and other breast cancer risk factors. In: Late Biological Effects of Ionizing Radiation. Vienna: International Atomic Energy Agency, p. 231-47, 1978; Shore RE, Woodard E, Hempelmann L, Pasternack B. Synergism between radiation and other risk factors for breast cancer. Prev Med 9:815-22, 1980).

Table 2 has a number of discrepancies between the ICD codes in the two columns. The basis for the discrepancies should be explained in footnotes or in the text.

For reasons given above and because there is no evidence to the contrary, differential radiation sensitivity for skin cancer in various ethnic populations should not be assumed -- the same ERRs per Gy are appropriate to apply to all populations. Therefore, Table 3 is not needed.