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From: Land, Charles (NCI) [mailto:landc@exchange.nih.gov]
Sent: Monday, November 26, 2001 10:55 AM
To: Elliott, Larry J. (CDC); Neton, Jim (CDC)
Cc: Gilbert, Ethel (NCI); Smith, James M. (CDC); Hoffman, Owen (E-mail); Duane, Betsy (NCI)
Subject: IREP

Dear Larry and Jim,

I'm writing to you today to give you some insights about our most recent plans to modify IREP and to express my desire to collaborate in order to achieve a consensus version of this code.

We plan to submit our PC tables revision report, and program, to NIH and DHHS in the very near future. Our version of IREP will differ in the following ways from the NIOSH IREP currently accessible on the web:

1) DDREF: The DDREF uncertainty distribution for breast and thyroid cancer will be replaced by a closely similar discrete distribution, but with 5% of the total probability shifted from DDREF values of 1 and above to the value 0.6.

This is in keeping with use of the continuous Grogan et al uncertainty distribution for DDREF for other solid cancers, which differs from the NCRP Report 126 uncertainty distribution by having 5% of the probability shifted from DDREF values of 1 and above, to values between 0.2 and 1.0. By allowing a small possibility that risk at low doses and dose rates may be higher, per unit dose, than at high doses and dose rates, the upper uncertainty limit for assigned share is increased.

2) Skin cancer: We asked Dale Preston, at RERF, to provide likelihood profile estimates of the uncertainty for excess relative risk of basal cell carcinoma for different exposure ages, and for the ERR of other non-melanoma skin cancers, a category that is mostly squamous cell carcinoma. The ERR estimate for the latter cancer group was negative and, because convergent estimates could not be obtained for different exposure ages, we settled for one without variation by exposure age. These uncertainty distributions will be incorporated into IREP. There are only 10 malignant melanomas in the RERF series so we did not include an estimate for that cancer. The estimate was not inconsistent with that for basal cell carcinoma.

3) Thyroid cancer: As you know, David Kocher's report recommended an uncertain RBE centering on 2.6 for 250 kVp X rays (low-energy photons) vs. the higher-energy gamma ray photons like those from the Hiroshima and Nagasaki bombs. Our thyroid cancer risk coefficients for childhood exposures are based mostly on patients exposed to X rays while the risk coefficients

for adults are based mostly on A-bomb survivor data. This would suggest defining RBE relative to low energy photons for evaluating exposure in childhood, and relative to high energy photons for evaluating exposure to adults.That hasn't been done before, and we will probably come up with a compromise that adds some more uncertainty to the estimates for childhood exposures related to cancers of the thyroid an other organs. This will not preclude making changes later, after your public comment has come in.

4) Bone cancer : We will not include estimates for bone cancer. There are only 15 cases in the RERF tumor registry data set; moreover, a convergent risk estimate could not be obtained, and we are informed that death certificate diagnoses of bone cancer in the LSS sample are unreliable (one of the reasons why the tumor registry series has so few bone cancer cases).

While the 1985 NIH report used the excellent data set from Spiess et al on bone sarcoma following injection of 224-Ra, this was something of a tour de force. The risks and dose distribution are very different between this very atypical exposure and those likely to have been experienced in occupational and military settings, and there seemed to be no good reason for including it again.

The current NIOSH IREP provides assigned share estimates for bone cancer and "residual and ill-defined tumors" that are fairly close for exposure at age 20, but differ by a factor of 2 or so for exposures at age 40. This discrepancy occurs largely because the residual tumor risk is modeled in terms of exposure age and age at diagnosis, while bone cancer is not. I can sympathize with your desire, and the VA's, to have a separate estimate for bone cancer, but this appears to be beyond us just as it was for the 1985 Ad Hoc Working Group.

I doubt that NIOSH will object to 1) or 3), and you would get about the same result for malignant melanoma as at present if you just used our basal cell carcinoma risks for malignant melanoma. That's an administrative decision. I expect that you may not agree with 4), although you would be justified in using the residual tumor estimates.

In retrospect, we have found that our interaction with NIOSH, and with Mary Schubauer-Berrigan in particular, was helpful to our report and our version of IREP. Also, David Kocher's report, which I understand NIOSH commissioned, is a substantial addition; we plan to include it as an Appendix to our report, if this is acceptable to you.

On the whole, I think it would be better to have a common version of IREP than to have two. However, I am also aware that more reasons for having a separate version of the code may surface, based upon comments you receive in the next few months. Nevertheless, I would like to extend to you my offer to collaborate in any way possible to find common ground so as to achieve a single version of IREP.

Yours sincerely,
Charles