

**Commentary by F. Owen Hoffman
on slides presented in the

Occupational Energy Research Program
Background and Mission
Public Meeting
October 27, 2005**

Slides by Teresa Schnorr

The mission of the Occupational Energy Research Program is very well articulated. This program should continue to be supported. Opportunities exist to answer outstanding research questions, provided that ample funding is secured to follow cohorts of relatively young age-groups. It is not clear to me what mechanisms NIOSH has to ensure that DOE will honor its obligations to fund analytic epidemiological research via the DHHS/DOE MOU. An independent advisory committee like ACERER might help alleviate some of the present problems that exist regarding future DOE funding.

In the absence of ACERER there needs to be an effective mechanism for oversight and input from stakeholders external to NIOSH and DOE. An independent oversight/advisory committee like ACERER would be instrumental in assuring the integrity/credibility of scientific objectives of OERP and research, as well as the relevancy of OERP research to the improvement of worker health.

Given the “benefit-of-the-doubt” and near-term objectives of Federal compensation programs, it is not clear to me how OERP research intends to interface with research needs of OCAS. Most OERP projects require many years of follow up, while OCAS requires information to support decisions that must be made on the time frame of months.

I would like to comment on each of the primary research questions:

(1) *Are current exposure limits adequate?* Given present epidemiological information and information from radiobiological research, combined with risk estimates from NIOSH-IREP and BEIR VII, I believe the answer to the above question is clearly, “no.” Individuals receiving doses that approach but do not exceed present day annual effective dose limits for workers could readily accumulate doses as high as 200 mSv in 5 years or 400 mSv over 40 years. These accumulated effective doses are estimated assuming an annual exposure of 40 mSv/y for 5 years, and assuming an annual exposure of 10 mSv/y over 40 years, respectively. These annual doses are below the annual occupational dose limits of 50 mSv/y. Cumulative doses on the order of 200 to 400 mSv would currently be sufficient to justify compensation for certain diagnosed cases of cancers that are currently considered for worker compensation under EEOICPA.

BEIR VII estimates that the lifetime health risk for an adult receiving 10 mGy/y from ages 18 to 65 would be associated with an increased risk of cancer of 1.5 to 6 chances in

100 for males and 2 to 8 chances in 100 for females (95% subjective confidence interval). These risks are much higher than cancer risks permitted for workplace exposures to chemical carcinogens.

(2) *What are the health risks for different forms of radiation?* Given the uncertainties associated with exposure quantification, and given the very low doses associated with most worker exposures at DOE sites, this question might not be answerable using epidemiological investigations as a sole source of information. It will be important to carefully examine the power of combined cohort studies before determining whether or not it is possible to detect differences in risk from different forms of radiation, when true differences may be less, say, than a factor of 2 to 3.

(3) *How do risks from fractionated exposures compare to risks from acute exposure?* Again, what is the statistical power of the study design? Is the power sufficient to detect a DDREF that may be greater than 1.0 but less than 2.0? To what extent will studies be subjected to confounding because cohorts are exposed to a variety of different radiation types, which include alpha emitters, low energy beta emitters, high energy photons, low energy photons, and neutrons? I suspect that it will be difficult to separate differences in risk due to contributions from different types of exposure and exposure to different radiation types. These differences could be masked by the effect of exposure fractionation or from chronic exposure to internal emitters that are associated with very low dose rates.

With regard to OERP communication goals, what are OERP's plans for the communication of radiation risk to workers and the public when planned and/or actual workplace exposures are below the limits of statistical significance in specific epidemiological studies? I believe that the Portsmouth Naval Shipyard study has successfully provided new evidence for the presence of radiogenic leukemia risks existing in worker populations exposed below a cumulative dose of 100 mSv.

What mechanisms will be put in place to evaluate whether or not OERP communication goals are met?

The slide on the potential impact of OERP research is excellent.

Slides by Doug Daniels

The important role of uncertainty when attempting to quantify exposures accurately cannot be overstated. Such uncertainty is present and inescapable. Uncertainty in dose estimation will affect the statistical power of an epidemiological study, as well as the slope and confidence intervals of the dose-response relationship.

Consider situations in which offsite exposures may be greater than onsite exposures (such as the ingestion of foodstuffs contaminated from fallout from nuclear weapons tests, or

onsite releases that contaminate offsite agricultural products that eventually are consumed at home or in the workplace).

Investigate the role that event-to-event, year-to-year correlations in dose uncertainties have on the interpretation of statistical power and dose-response relationships. This may be particularly important for internal emitters.

Statistically insignificant results are not evidence of the absence of risk. I recommend that NIOSH restate research questions for which a 'no' answer cannot be obtained with direct epidemiological observation. The question, "Does chronic, low-level exposure cause leukemia among workers?" cannot be answered in the negative by an epidemiological study that, although statistically insignificant, has wide confidence intervals about the regression line of the dose-response or about the relative risk at a given average level of dose.

LCCS Unique Aspects

Although combined cohort studies may be most informative about CLL dose-response, I question whether there will be sufficient power to answer the question, "Is CLL associated with radiation," even when the combined number of CLL is as high as $n=43$. I say this in the anticipation that the true dose-response relationship for CLL may not be as steep as is the case for other radiogenic leukemias, and may in fact be more in line with non-Hodgkins lymphoma.

Portsmouth Naval Shipyard Lung Cancer Case Control Study

Again, the absence of a statistically-significant dose response cannot be construed as evidence for the absence of risk. I do not believe that it is possible for epidemiological studies alone to answer the question, "Does chronic low-level radiation exposure cause lung cancer among workers?" Given our current state of knowledge, the answer to this question is clearly, "yes."

Impact of Ongoing OERP Research.

In the future, will OERP be giving more weight to confidence intervals on the dose-response relationship than to the significance of p -values?

To what extent will the result of OERP research be put into perspective with other epidemiological radiation research conducted outside of OERP (NCI and international studies) and with recent findings in radiobiology, as well as the conclusions of BEIR VII?

To what extent will the findings from OERP be used to establish guidelines for improved limits on workplace exposures in the medical industry?

Slides by Travis Kubale

As with previous presentations, I am concerned about the absence of a statistically-significant dose response or relative risk being misrepresented as a finding of “no association” or “no excess cancer risk.” In most all cases, the presence of a statistically insignificant finding (or $p > 0.05$), or the presence of confidence intervals that overlap zero risk, cannot be used to prove the presence of a negative outcome. The upper bounds of these confidence intervals must also be taken into account. This is especially important given the conclusions of the recent BEIR VII report, that there is no dose below which there is no increased risk.

In discussing the observed health effects from low-level chronic and/or fractionated radiation exposures, it will be useful to compare results of values of DDREF proposed by BEIR VII and in NIOSH IREP with the outcomes anticipated from NIOSH OERP epidemiological investigations.

Overall, the presentation was in-depth and very well done. An excellent use of PowerPoint.

Slides by Mary Schubauer-Berigan

An overall excellent presentation and a nice example of the use of PowerPoint as a communication tool.

OERP Research Agenda: External Influences

How will OERP answer the following questions?

- (a) “Is CLL risk associated with cancer?”
- (b) “How does radiation interact with smoking in causing lung cancer?”
- (c) “How does radiation interact with other workplace exposures?”

These, of course, are questions being raised by OCAS, but I’m not sure that OERP has a straightforward approach to answer these questions.

With respect to BEIR VII, the answer to the question, “Does chronic low-level radiation cause cancer?” should clearly be, “yes.” If not, what methods are being proposed by OERP to demonstrate a negative answer to this question? What methods will OERP use to distinguish between underlying true levels of DDREF of 0.5, 0.7, 1.0, 1.5, and 2.0, which may be masked by errors in dosimetry and low statistical power?

I believe that the uncertainty in the dose-response analysis will be such (when all sources of uncertainty are taken into account) that it may be difficult to determine differences in DDREF on the order of the values I have given above.

Thank you for a very fine set of presentations and for the opportunity to participate in your public meeting. Your research is important, and your program should continue to be funded. I hope that my written comments are useful for future evaluation of your research priorities. Please let me know if and when I can be of help in the future. If there is a need for me to clarify anything that I have submitted with this commentary, please do not hesitate to contact me.

Sincerely,

Owen Hoffman