National Institute for Occupational Safety and Health

NIOSH

Comments to NRC

Comments of the National Institute for Occupational Safety and Health on the Nuclear Regulatory Commission Notice of Docketing and Request for Comment on Linear No-Threshold Model and Standards for Protection Against Radiation

Docket Nos. PRM-20-28, PRM-20-29 and PRM-20-30; NRC-2015-0057

Department of Health and Human Services
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
Cincinnati, Ohio

September 11, 2015

The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Nuclear Regulatory Commission (NRC) *Linear No-Threshold Model and Standards for Protection Against Radiation*, a notice of docketing and request for comment on three petitions for rulemaking (i.e., Docket Nos. PRM-20-28, PRM-20-29, and PRM-20-30; NRC-2015-0057) published in the *Federal Register* (FR) on June 23, 2015 [80 FR 35870].

NIOSH recommends that the NRC not adopt the petitioners' request to drop the use of the "Linear No-Threshold" (LNT) model in its protective standards for workers. The following comments are intended to assist the NRC in responding to the petitioners.

Introduction

An estimated 22.8 million workers worldwide are exposed to ionizing radiation during their work: 13 million to natural sources and about 9.8 million to man-made sources [UNSCEAR 2008, p. 13]. Medical workers comprise 75% of the latter group. Thus, an understanding of the health effects from low doses of ionizing radiation, particularly cancer, is an important occupational health topic. The risks associated with exposure to low levels of ionizing radiation were considered by the U.S. National Academies in its series of reports on the Biological Effects of Ionizing Radiation (BEIR). The most recent report of the BEIR committees, the BEIR VII report [National Academies 2006], considered the health effects of exposure to low linear energy transfer (LET) radiation, such as gamma and x-rays. The BEIR VII committee thoroughly considered the scientific validity of non-LNT models in describing cancer risk from low doses of ionizing radiation. However, the committee rejected these non-LNT models in favor of the traditional assumptions that risk declines linearly with decreasing dose for most cancers, and that there is no practical "threshold" that can be established when the cancer risk is zero. The lines of evidence given by the petitioners are not new and are fundamentally the same as those rejected by the BEIR VII committee [National Academies 2006, Appendix D].

Occupational epidemiologic studies of low-dose cancer risk published since the BEIR VII report

Since the 1970s, NIOSH has conducted research on the health effects of exposure to external and internal forms of workplace ionizing radiation. Many early studies of nuclear workers and others exposed to low doses of ionizing radiation had equivocal results. A frequent pattern was a positive risk estimate that was too imprecise to rule out no effect [Schubauer-Berigan et al. [2007]]. This occurred because large numbers of workers and lengthy follow-up are required to observe a significant positive dose-response pattern at the low cumulative doses that workers typically receive [National Research Council 2006].

NIOSH researchers and others conducted meta-analyses of cancer risk from low-dose exposures in a variety of populations receiving protracted exposure to external ionizing radiation [Jacob et al. 2009; Daniels and Schubauer-Berigan 2011]. These meta-analyses concluded that there is a small but significant excess risk of solid cancer and leukemia, respectively, at occupational doses received during a typical working lifetime [Walsh 2011].

More recently, NIOSH researchers and others published two important studies describing cancer risk among nuclear workers. A pooled cohort study (with updated mortality information) included nearly 120,000 nuclear workers from five sites: four U.S. Department of Energy (DOE) sites (Hanford, Idaho National Laboratory, Oak Ridge National Laboratory, and Savannah River Site) and the Portsmouth Naval Shipyard [Schubauer-Berigan et al. 2015]. The excess relative risk (ERR) was significantly

associated with occupational radiation dose for all non-smoking-related cancers combined (ERR/Sievert (Sv): 0.70, 95% confidence interval (CI): 0.058, 1.5), and for all lymphatic and hematopoietic cancers combined (ERR/Sv: 2.0, 95% CI: 0.71, 3.5) [Schubauer-Berigan et al. 2015]. These findings suggest that the risk of these cancers rises by 0.7% and 2.0% (respectively) for every 10 millisieverts (mSv) increase in dose. The average dose among the cohort was 20 mSv.

Secondly, an international nuclear workers (INWORKS) study included the pooled U.S. nuclear worker cohort described above, and large pooled nuclear worker cohorts from France and the United Kingdom [Hamra et al. 2015; Leuraud et al. 2015; Thierry-Chef et al. 2015]. The INWORKS study encompassed the largest and most informative cohorts from the 15-country study, and included extended mortality follow-up for each country. It included more than 300,000 workers and 531 leukemia (other than chronic lymphocytic) deaths (compared to 196 in the 15-country study by Cardis et al. [2005]). The average whole-body dose was 25.2 mSv [Thierry-Chef et al. 2015]. The study found a significantly elevated risk of leukemia (excluding chronic lymphocytic) (ERR/Gray (Gy): 2.96 (90% CI: 1.17, 5.21) [Leuraud et al. 2015]). This point estimate changed little when the data were restricted to a dose range of 0 to 300 milligray (mGy) or 0 to 100 mGy to the red bone marrow or in other sensitivity analyses.

These recent findings from large, well-conducted epidemiologic studies of workers receiving low-dose ionizing radiation exposure are supportive of the continued use of the LNT model and "as low as reasonably achievable" (ALARA) principles as a reasonable framework for protecting workers from excess risks associated with occupational exposure to ionizing radiation.

The comments below focus on aspects of the petitions that relate to either occupationally exposed populations (e.g., nuclear shipyard workers), or to groups whose exposure has been highly influential in the development of radiation protection standards (e.g., Japanese survivors of the atomic bombings in World War II). The petition by Miller (PRM-20-29) largely reiterates points made by Marcus (PRM-20-28) and Doss (PRM-20-30). To avoid redundancy, we did not respond directly to the petition by Miller (PRM-20-29).

<u>Comments on incoming petition for rulemaking from Carol S. Marcus (PRM-20-28)</u>

1. The petitioner cited a recent study of the Japanese atomic-bomb survivors, Ozasa et al. [2012], as evidence of an hormetic effect from ionizing radiation exposure for all solid cancers in the low dose range (0.3-0.7 Gy) among survivors. However, the authors found that the dose-response slope was "*nominally higher at doses below 0.1 Gy*" (Ozasa et al. [2012], page 238 and figure 5) compared to higher doses. In fact, the lowest dose range with a statistically significant ERR for all solid cancer was 0 to 0.20 Gy with an estimated ERR of all-solid cancer mortality per Gy of radiation dose of 0.56 (95% CI: 0.15, 1.04) in this range [Ozasa et al. 2012]. This point estimate is greater than the estimate obtained over the entire dose range (0.47; 95% CI: 0.38, 0.56), although confidence intervals overlapped.

2. In the discussion of leukemia incidence among Japanese atomic bomb survivors, the petitioner omitted an important study by Hsu et al. [2013] of the dose-response relation between radiation exposure and leukemia incidence. In this authoritative study, data were fit to several dose-response functions, including models that allowed for a dose threshold. Although temporal patterns and shapes of the dose-response differed by leukemia subgroups, there was no evidence of a risk threshold or protective effect for any outcome examined. The preferred ERR model for leukemia (excluding the chronic lymphocytic and adult T-cell subtypes) was linear-quadratic in dose.

3. The petitioner stated incorrectly that the study of radiation workers in 15 countries (Cardis et al. 2007) "showed a decrease in the risk of all cancers including leukemia." In fact, Cardis et al. [2007] reported increasing all-cancer risk with dose. The ERR of all-cancer mortality per Sv of radiation dose was 0.97 (90% CI: 0.28, 1.77) [Cardis et al. 2007]. The point estimate was unchanged by removing leukemia (0.97; 90% CI: 0.27, 1.80). After publication, questions arose regarding the influence of the Canadian data on this point estimate. Removing Canadian data reduced the ERR for all cancers excluding leukemia to 0.58 (90% CI: -0.10, 1.39), a positive result, although not statistically significant [Cardis et al. 2007]. Cardis et al. [2007] also conducted analyses restricting doses to different levels. The lowest cumulative dose level with a statistically significant ERR for all cancers excluding leukemia was <0.15 Sv (ERR/Sv =1.39; 90% CI: 0.02, 2.92).

4. The petitioner stated that the BEIR VII Report [National Academies 2006] incorrectly suggested that a "*mysterious effect*" known as a healthy worker effect was the likely explanation of deficits in mortality often observed among radiation workers compared to a referent population. Contrary to the petitioner's assertion, the healthy worker effect (HWE) is a well-known effect in longitudinal studies of workers and was explained in several seminal books on study methods [Checkoway et al. 2004; Rothman et al. 2008; Breslow and Day 1987]. Given rigorous medical qualifications for radiation work (e.g., Baillargeon 2001), HWE likely explains deficits in mortality compared to external referent populations, which was referenced in the BEIR VII report. Furthermore, this effect is not unique to radiation-exposed populations; nearly all studied working populations tend to exhibit the HWE. Employment provides improved access to health care, continued health screening, and income and psychosocial benefits, which benefit health status [Baillargeon 2001; Checkoway et al. 2004; Waddell and Burton 2006; Robert Wood Johnson Foundation 2013].

The petitioner states that the HWE is "*actually backwards*" (i.e., that cancer rates should be higher among working populations). The basis provided by the petitioner appears to be that healthy workers reach a higher attained age compared to the referent population; therefore, workers should have a greater probability of a stochastic disease. This idea is without merit because study effect measures (e.g., rate ratio, standardized mortality ratios (SMRs)) are age-adjusted. In existing epidemiologic studies of radiation workers, the study populations tend to be young, even in recent studies with long observation periods. For example, the mean age at end of observation in the recent pooled study of over 300,000 nuclear workers from France, the United Kingdom, and the United States was 58 years; less than 22% of the cohort was deceased at the end of study [Hamra et al. 2015].

Comments on incoming petition for rulemaking from Mohan Doss et al. (PRM-20-30)

1. As evidence of protective effects of radiation exposure, the petitioner cited a nuclear shipyard worker study (Sponsler and Cameron 2005) of radiation workers with radiation dose of about 0.04 Gy and significantly lower cancer mortality rates compared with workers from the same shipyard with no occupational radiation dose. Reference 20 provided by the petitioner is a review of the unpublished report; results from external and internal comparisons were published later [Matanoski et al. 2008]. Adjusted all-cancer mortality rates by groups were not formally compared in the petitioner's reference; therefore, the claim that cancer mortality risks among nuclear workers were "significantly lower" when compared to nonnuclear workers is unsubstantiated. Nevertheless, it is reasonably clear that nonnuclear workers had increased mortality risk compared to nuclear workers. This finding is unremarkable given that shipyard nuclear workers must undergo rigorous health screening to be selected and maintain

qualification as radiation workers. Furthermore, nuclear submarine jobs require specialized training and are typically performed by workers with higher seniority and skill levels. As a result, nonnuclear shipyard workers tend to be less healthy and have shorter careers compared to nuclear workers [Matanoski et al. 2008]. This health difference may be attributable to differences in risk factors other than ionizing radiation exposure. Lower death rates for non-malignancies such as emphysema, arteriosclerotic heart disease, and cirrhosis of the liver (outcomes not generally associated with ionizing radiation exposure) among nuclear workers in this cohort point to potential differences in lifestyle that may influence cancer risk. The radiation workers exposed to less than 5.0 mSv compared to the U.S. male population had excess lung cancer mortality (SMR=1.11, 95% CI: 0.90, 1.35) [Matanoski et al. 2008]. More importantly, the relative risk estimates among nuclear shipyard workers in the highest exposure category (i.e., >50 mSv) compared to workers with doses <10 mSv were 2.41 (95% CI: 0.5, 23.8) for leukemia, 2.94 (95% CI: 1.0, 12.0) for all lymphatic and hematopoietic cancers combined, and for lung cancer, 1.26 (95% CI: 0.9, 1.9). The study authors concluded that these findings were evidence of a positive association between radiation dose at occupational levels and cancer.

2. The petitioner argued that the upward curvature in dose-response observed in the recent analysis by Ozasa et al. [2012] of solid cancer mortality in Japanese atomic bomb survivors restricted to doses <2.0 Gy is compelling evidence of radiation hormesis. Although the model fit improved using a linear-quadratic (LQ) rate function rather than a linear function in this dose range, the linear component of the model remained positive (i.e., indicating excess risk). Thus, it is unclear how this finding supported the petitioner's argument. As correctly indicated by the petitioner, the upward curvature in ERR was attributed to lower than expected risks (based on a linear model) in the dose range 0.3–0.7 Gy [Ozasa et al. 2012, figure 4]. The petitioner did not mention that estimated ERRs under 0.3 Gy were "nominally higher than the best-fitting linear slope or the LQ function for either 0-2 Gy or the full dose range" [Ozasa et al. 2012, page 235].

3. The petitioner stated that the threshold analysis by Ozasa et al. [2012] was flawed because *"…it used a restricted functional form for dose response that did not cover the full range of the observed data.*" It should be noted that the analyses cited in support of the petitioner's argument in the immediately preceding paragraph also used restricted data (i.e., data restricted to dose <2.0 Gy). Perhaps the petitioner was concerned that analyses using a linear or LQ rate function may be too restrictive to illustrate the dose response at low doses. To address a similar concern in data restricted to <2.0 Gy, a quadratic-spline function was fit with a knot at 0.2 Gy; however, the model did not fit significantly better than the LQ function (P=0.16) and did not support a reduction in risk below this dose level.

4. The petitioner recommended a dose threshold (100 mSv), but the basis for the value is unclear.

5. The petitioner's recommendation to keep worker doses at present levels contradicts the removal of ALARA, because the present levels, in part, are a consequence of current ALARA practices.

Overall comments in response to the three petitions for rulemaking

Changes to U.S. radiation protection standards have been predicated on careful consideration of recommendations from respected national and international bodies of experts, such as the National Research Council of the National Academies, the National Council of Radiation Protection & Measurements (NCRP), the International Atomic Energy Agency (IAEA), and the International Committee on Radiation Protection (ICRP). To date, none of these organizations have recommended the

use of a threshold or hormesis model in assessing radiation risk for protection purposes even though much of the information provided in the three petitions has been available for their consideration. Until these organizations agree that the weight of evidence justifies reexamination of the LNT model, retaining the current standards for radiation safety is recommended.

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NRCExecSec Resource

From:	Toye, Sally (CDC/OD/OCS) <slc0@cdc.gov>
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To:	NRCExecSec Resource
Cc:	Spring, Christina M. (CDC/NIOSH/OD); Toye, Sally (CDC/OD/OCS); Rice, Faye L. (CDC/NIOSH/EID)
Subject:	CDC/NIOSH comments on Linear No-Threshold Model and Standards for Protection against radiation [NRC]
Attachments:	NRC LNT petitions-NIOSH comments v10-for CDC review.docx

Good morning:

The Centers for Disease Control and Prevention's (CDC) National Institute for Occupational Safety and Health (NIOSH) has reviewed the Nuclear Regulatory Commission (NRC) *Linear No-Threshold Model and Standards for Protection Against Radiation*, a notice of docketing and request for comment on three petitions for rulemaking (i.e., Docket Nos. PRM-20-28, PRM-20-29, and PRM-20-30; NRC-2015-0057) published in the *Federal Register* (FR) on June 23, 2015 [80 FR 35870].

NIOSH recommends that the NRC not adopt the petitioners' request to drop the use of the "Linear No-Threshold" (LNT) model in its protective standards for workers. The attached comments are intended to assist the NRC in responding to the petitioners.

We would very much appreciate your forwarding to the appropriate SMEs for their consideration. Please note that these comments are for consideration only, and not for the public docket. Please contact me at 404-639-7082 should you have any concerns or comments. Thank you.

Sally Toye
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Centers for Disease Control and Prevention