

**Report to the Senate Appropriations Committee on
The Radiogenicity of Specific Cancers
Under the Energy Employees Occupational Illness
Compensation Program Act of 2000 as Amended**

National Institute for Occupational Safety and Health

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SUMMARY

In response to Senate Report (S. Rep.) 109-103 (2005), NIOSH examined the evidence for the radiogenicity¹ of 11 “non-presumptive cancers” which were not included in the list of 22 “specified cancers” referenced in the Energy Employees Occupational Illness Compensation Program Act of 2000 as amended (EEOICPA)². Based on a review of relevant scientific publications, NIOSH finds consistent evidence to support the radiogenicity of basal cell carcinoma. As requested in Senate Report 109-103, this report enumerates cases of basal cell carcinoma among classes of employees included in the Special Exposure Cohort (SEC). This is an interim report to Congress because it is expected that soon the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) will issue a new report summarizing comprehensive reviews of latest scientific findings. Based on examination of the findings from the new UNSCEAR study and other relevant information, NIOSH will issue a final report to Congress.

RADIOGENICITY OF SPECIFIC CANCERS

Comprehensive reviews of the radiogenicity of various specific cancers appeared in the peer-reviewed scientific literature in the mid- and late 1990s (Boice et al. 1996, Mettler and Upton 1995, Ron 1998). The most extensive recent examination of this topic was published by UNSCEAR (2000). These four reviews reflect the weight of the available scientific evidence

¹ Radiogenicity refers to the causation of cancer in a given organ by exposure of that organ to ionizing radiation.

² The Department of Labor treats colon and rectal cancer as one type of cancer for purposes of EEOICPA, based on a National Cancer Institute advisory.

and are less prone than individual epidemiologic studies to reaching conclusions based on chance associations.

The current classification under EEOICPA for site-specific cancers is found in Table 1.

The table presents cancers in specific organs individually, including those that are grouped in the NIOSH Interactive Radioepidemiology Program (NIOSH-IREP) as “other respiratory,” “other endocrine,” and “other and ill defined sites.”

Table 2 summarizes the primary conclusions of the four comprehensive reviews regarding the radiogenicity of each current non-presumptive site-specific cancer listed in Table 1. The four reviews differed in the list of cancers explicitly considered. To the extent that specific cancers were discussed, the authors were similar in concluding that little or no evidence of radiogenicity exists for chronic lymphocytic leukemia (CLL) and cancers of the connective tissue, larynx, lymphoma (Hodgkin’s), male genitalia, oral cavity, prostate, and uterus.

The scientific evidence for skin cancer is more complicated, depending on the specific type of skin cancer. UNSCEAR (2000) recognized a strong relationship between radiation and basal cell carcinoma, but reported little evidence of an association for squamous cell carcinoma or malignant melanoma.

In a study focused on the Japanese atomic bomb survivors, Ron et al. (1998) reached conclusions similar to those of UNSCEAR. In this study, there was a pronounced decrease in the excess

relative risk (ERR)per Sievert (ERR/Sv) for BCC as age increased, however, the risk remained significant at the 90% confidence interval for those who were exposed up to 39 years of age.

Shore (2001) also examined the evidence of an association between skin cancer and ionizing radiation exposure, and his conclusions are consistent with those of Ron et al. (1998) and UNSCEAR (2000). In addition to the Japanese life span study, Shore reviewed other studies which provide evidence that BCC is related to exposure to ionizing radiation. These include evaluations of radiologists, uranium miners, and patients exposed during medical treatments. Shore (2001) concludes that:

The principal epidemiological studies of ionizing radiation and skin cancer have all shown that radiation causes basal cell carcinoma but have not found dose-related excesses of squamous cell carcinoma or malignant melanoma.

A summary of the findings of the studies reviewed by Shore is provided in Table 3.

In contrast to these findings, a recent review argued for an association between radiation and malignant melanoma (Fink and Bates 2005). This review employed meta-analytical techniques to examine melanoma risks relative to leukemia risks in populations which may have been exposed to ionizing radiation. The report concluded that:

people exposed to ionizing radiation may be at increased risk of developing melanoma, although alternative explanations are possible. Future epidemiological studies of ionizing radiation effects should include melanoma as an outcome of interest.

Both Mettler and Upton (1995) and Boice et al. (1996) discussed skin cancer as a single entity, with the former indicating that a number of studies show an association with radiation, and the latter concluding that skin cancer is rarely associated with radiation and effects may be limited to high doses. Ron (1998) also considered skin cancers as a group and concluded that associations have been reported but are not well quantified.

More recently, the United States National Academy of Sciences published *Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2* (National Research Council 2006), which does not explicitly discuss the evidence of radiogenicity for specific cancers, but notes that nonmelanoma skin cancer has been linked clearly with radiation exposure in atomic bomb survivor data.

Taken together, NIOSH finds consistent evidence to support the radiogenicity of basal cell carcinoma, but not malignant melanoma. As previously noted, the evidence of radiogenicity of basal cell carcinoma is much stronger for exposures received at young ages, particularly during childhood. The strength of the association declines with age, becoming statistically insignificant among most populations exposed at older ages (UNSCEAR 2000). Additionally, it is recognized that a primary cause of basal cell carcinoma is exposure to ultraviolet radiation in sunlight (UNSCEAR 2000). The nature and magnitude of the interaction between ultraviolet and ionizing radiation exposure are unknown at this time (Shore 2001, UNSCEAR 2000).

CONCLUSION

Review of the evidence of radiogenicity of specific cancers indicates that there is strong epidemiologic evidence for the radiogenicity of basal cell carcinoma and insufficient evidence for larynx, CLL, lymphoma (Hodgkin's), male genitalia, oral cavity, prostate, skin (squamous cell), uterus, and malignant melanoma. This interim report will be updated when UNSCEAR releases a new report.

REFERENCES

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7. Shore RE. Radiation-induced skin cancer in humans. *Med.Pediatr.Oncol.* 36:549-554; 2001.
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Table 1: Current presumption status of specific cancers under EEOICPA^a

Cancer Site	Presumption Status
Bile ducts	Presumptive
Bone	Presumptive
Brain	Presumptive
Breast	Presumptive
Colon/rectum ^b	Presumptive
Connective tissue	Non-presumptive
Esophagus	Presumptive
Gall bladder	Presumptive
Kidney	Presumptive
Larynx	Non-presumptive
Leukemia (exc. CLL)	Presumptive
Liver	Presumptive ^c
Lung	Presumptive
Lymphoma (NHL)	Presumptive
Lymphoma (Hodgkin's)	Non-presumptive
Male genitalia	Non-presumptive
Multiple myeloma	Presumptive
Oral cavity	Non-presumptive
Ovary	Presumptive
Pancreas	Presumptive
Pharynx	Presumptive
Prostate	Non-presumptive
Salivary gland	Presumptive
Skin – BCC	Non-presumptive
Skin – SCC	Non-presumptive
Skin – melanoma	Non-presumptive
Small intestine	Presumptive
Stomach	Presumptive
Thyroid	Presumptive
Urinary bladder	Presumptive
Uterus	Non-presumptive

CLL = chronic lymphocytic leukemia

NHL = non-Hodgkin's lymphoma

BCC = basal cell carcinoma

SCC = squamous cell carcinoma

a: To qualify as presumptive under the SEC, most cancers require a minimum time period of 5 years between first exposure to radiation and cancer diagnosis. The exceptions are bone, lung, and kidney cancer (no minimum) and leukemia (minimum = 2 years).

b: The Department of Labor's Employment Standards Administration (ESA) noted that the National Cancer Institute considers rectal cancer to be the same as colon cancer based on tissue similarity, and thus groups the two together as colon/rectal cancer. Therefore rectal cancer is considered to be the same cancer as colon cancer for ESA purposes, and is treated as a specified cancer for EEOICPA purposes.

c: Liver cancer is considered presumptive except when cirrhosis or hepatitis B is indicated.

Table 2: Evaluation of radiogenicity of currently nonpresumptive cancers in comprehensive reviews

	(Mettler and Upton 1995)	(Boice <i>et al.</i> 1996)	(Ron 1998)	(UNSCEAR 2000)
Connective tissue	NA	Rarely associated with radiation with no reliable risk estimates available. Effect may be limited to high doses.	NA	NA
Larynx	“The oral cavity, pharynx and larynx are generally regarded as tissues of low risk in radiation carcinogenesis”.	NA	NA	NA
Lymphoma (Hodgkin’s)	“With the exception of what are thought to be statistical chance associations radiation has not been associated with the development of Hodgkin’s disease”.	Hodgkin’s never or sporadically associated with radiation with no risk estimate. Little evidence.	“...rarely related to radiation exposure”.	“...the available data do not indicate an association between Hodgkin’s disease and radiation, either for external or internal exposures”.
Male genitalia	“The epidemiologic literature shows no causal association between male genital cancer and radiation exposure”.	Never or sporadically associated with radiation with no risk estimates. Little or no evidence.	“...rarely related to radiation exposure”. (testes)	NA
Oral cavity	“Epidemiologic studies show no consistent or statistically significant increase in cancer of the oral cavity or pharynx following internal or external radiation exposure”.	NA	NA	NA
Prostate	“A large number of epidemiologic studies have looked for an increased risk of prostate cancer after radiation exposure. At the present time there is no clear evidence that prostate cancer is induced by radiation”.	Never or sporadically associated with radiation with no risk estimates. Little evidence.	“...rarely related to radiation exposure”.	“Data from the Japanese atomic bomb survivors and from most other studies provide little evidence of an elevated risk of prostate cancer following radiation exposure”.
Skin - BCC	“A number of studies indicate an association between skin cancer and	Rarely associated with radiation with uncertain risk	“Associations between radiation and cancer...have	“Ionizing radiation can induce non-melanoma skin

	(Mettler and Upton 1995)	(Boice <i>et al.</i> 1996)	(Ron 1998)	(UNSCEAR 2000)
	radiation”.	estimates. Effect may be limited to high doses.	been reported, but the relationships are not as well quantified”.	cancer but the relationship is almost entirely due to a strong association with basal-cell carcinoma”.
Skin – SCC, malignant melanoma	“A number of studies indicate an association between skin cancer and radiation”.	Rarely associated with radiation with uncertain risk estimates. Effect may be limited to high doses.	“Associations between radiation and cancer...have been reported, but the relationships are not as well quantified”.	“To date there has been little indication of an association between ionizing radiation and malignant melanoma or squamous-cell carcinoma, but the data are sparse”.
Uterus	“The epidemiologic literature does not support radiation induction of uterine neoplasms”.	Rarely associated with radiation with uncertain risk estimates. Effect may be limited to high doses.	“...rarely related to radiation exposure”. (cervix)	NA

NA = this cancer was not explicitly considered

BCC = basal cell carcinoma

SCC = squamous cell carcinoma

Table 3: Studies of Ionizing Radiation and Skin Cancer Risk (from Shore 2001)

Study	Relative Risk (at 1 Gray or Sievert)	95% Confidence Interval
Japanese atomic bomb	2.8	1.8-4.3
Israel tinea capitas	1.7	1.3-2.4
New York tinea capitas X-ray	1.6	1.3-2.0
Enlarged thymus X-ray	2.1	1.4-3.0
Lymphoid tissue X-ray	1.2	1.1-1.7
Enlarged tonsils X-ray	1.1	1.0-1.2
Uranium miners	2.1	1.7-2.7
TB fluorospcopy	1.0	<1-1.0
Postpartum mastitis X-ray	1.1	<1-1.4

Table 4: Number of basal cell carcinoma claims at each currently-designated SEC site (as of June 5, 2007)

SEC ³ Site (and time period covered by the approved SEC class)	Number of claims with basal cell carcinoma as a listed cancer
Allied Chemical (1/1/59-12/31/78)	24
Amchitka Island Nuclear Explosion Site (before 1/1/1974)	36
Ames Laboratory (1/1/42-1/31/54)	6
General Atomics (1/1/60-12/31/69)	18
Harshaw Chemical (1/1/42-11/30/49)	0
Iowa Ordnance Plant (3/1949-12/1974)	96
Los Alamos National Laboratory (9/1/44-7/18/63)	74
Linde Ceramics Plant (10/1/1942 – 10/31/1947)	54
Mallinckrodt Chemical Works, Destrehan Street Facility (1942-1957)	82
Monsanto (1/1/43-12/31/49)	2
Nevada Test Site (1/27/51-12/31/62)	96
Oak Ridge Gaseous Diffusion Plant (K-25 Site) (before 2/1/1992)	372
ORINS (5/15/50-12/31-63)	3
Pacific Proving Ground (1946-1962)	19
Paducah Gaseous Diffusion Plant (before 2/1/1992)	481
S-50 Thermal Diffusion Plant (7/9/44-12/31/51)	3
Portsmouth Gaseous Diffusion Plant (before 2/1/1992)	290
Y-12 Plant (3/1943-12/31/1957)	329

³ Special Exposure Cohort