Sabella.AnnaLee

From: Jameson.Bill
Sent: Tuesday, September 25, 2001 9:47 AM
To: Sabella.AnnaLee
Cc: Lunn.Ruth; Jeter.Shawn
Subject: FW: Comments for the Eleventh Edition of the Report on Carcinogens

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From: Cindy Folkers
Reply To: cindyf@nirs.org
Sent: Monday, September 24, 2001 05:16 PM
To: jameson@niehs.nih.gov
Subject: Comments for the Eleventh Edition of the Report on Carcinogens

Card for Cindy Folkers

Nuclear Information & Resource Service
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202-328-0002 phone
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Dr. C.W. Jameson
National Toxicology Program

VIA e-mail

September 24, 2001

Dear Dr. Jameson,

Thank you for the opportunity to comment on consideration of three forms of ionizing radiation for listing as reasonably anticipated or known human carcinogens in the Eleventh Edition of the Report on Carcinogens.

Following are summaries of studies investigating effects on human and
cell populations from gamma-rays, x-rays, and neutrons. Evidence exists
that all forms of ionizing radiation are carcinogenic, not just the ones
you have chosen for investigation. Alpha and beta particles also cause
cancer and we strongly recommend that you list these radiation types as
known carcinogens. We will formally submit references on this point at a
later time. Due to the tragedies of September 11, research facilities
have been difficult to access or simply unavailable. We would like
additional time to comment which we believe to be available based on our
phone conversation earlier last week. Therefore, we will add further
comments concerning gamma, x-rays and neutrons. Where possible, we
include not only the reference of the studies, but the studies
themselves.

Significant numbers of people are exposed to all ionizing radiation
types. While many humans are subjected to gamma-rays, x-rays, and
neutrons from medical diagnosis and treatments, these exposures end with
the patient and the patient's family. In addition to minimizing medical
exposures, we must recognize and curtail the daily environmental
contamination which exposes us to additional and long-lasting radiation
doses. Ionizing radiation is spewed daily from the entire nuclear fuel
chain including nuclear reactor operations such as at reprocessing
facilities and power reactors and weapons fabrication facilities.
Workers and members of the public are being exposed continually and over
generations as a result of release of man-made radionuclides to our

environment which do not simply vanish conveniently with the current
generation. Many of the studies summarized and referenced here consider
human disease in and around such facilities.

Ionizing radiation causes cancer. This is not disputed and while we welcome the NTP consideration to list these carcinogens, we also think
it is about time. Throughout the scientific literature, there are statements like 'there is not safe dose of radiation', 'there is no dose of radiation below which a negative effect is not seen', "the well-recognized role played by ionizing radiation in the development of
certain other forms of malignant diseases can be extended to include
carcinoma of the breast...(MacKenzie, 1965)", radiation is a general carcinogen. (Please see our sheet of compiled quotes from eminent scientists and researchers on the dangers of even low levels of ionizing
radiation). More importantly, the human and cell data illustrated by scientific studies support the fact that ionizing radiation causes cancer. Further, a low dose of radiation does not diminish the risk involved. Some studies show that lower doses actually pose more danger
per unit dose than higher doses. Since NTP is only considering whether
something is a potential or known carcinogen and is not considering dose
or risk, we have not compared the low-dose risk and high-dose risk of
cancer causation. However, it is important to note that low-doses of the
radiation types in question have been linked with cancer and, further,
these doses are within the range of doses not just to workers, but to

members of the general public as well. These members include unborn and
young children who studies have found are particularly susceptible to
radiation.

Not only do these studies show that ionizing radiation causes cancer, many are starting to reveal the cellular mechanisms that allow this to
happen at both the cellular and the organism level. Some studies indicate the ability of ionizing radiation to cause genomic instability which leads to cancer in future generations of both cells and humans; in
the case of some cell cultures, the actual radiation dose was not delivered to the precursor of the damaged cells, but only to neighboring
cells.

Evidence for carcinogenicity of X-RAYS

Human

*1) Court Brown, W.M., Richard Doll. "Mortality from Cancer and Other
Causes after Radiotherapy for Ankylosing Spondylitis. BMJ 1965,2. 1327-1332. AND FOLLOW-UP:
*2) Weiss HA, Darby SC, Fearn T, Doll R. "Leukemia mortality after X-ray
treatment for ankylosing spondylitis" Radiat Res 1995 Apr;142(1):1-11
Population: Patients treated for Ankylosing Spondylitis with x-rays.
Follow up-time: 5-25 years based on patients; disease end point: Death
Total deaths from Cancers expected 133.25; Deaths observed: 267
Aplastic Anemia: .51 expected; 15 Observed
Leukaemia: 5.48 expected; 52 Observed
Other cancers of irradiated sites: expected: 127.27; 200 observed

The researchers estimate that "...in an average follow-up period of 13
years after first treatment the excess deaths from leukaemia and from
other cancers arising in heavily irradiated tissues, which can be attributed to the effects of ionizing radiations, were 4 per 1,000 patients and 6 per 1,000 patients respectively."

"There is, however, no known factor other than radiotherapy which could
account for an increase in so many different types...It remains a possibility, however, until a sufficient series of observations have been made on patients treated by other methods."

And as a follow-up study in 1995 concludes:

"Leukemia mortality has been studied in 14,767 adult ankylosing spondylitis diagnosed between 1935 and 1957 in the United Kingdom, of
whom 13,914 patients received X-ray treatment. By 1 January 1992, there
were 60 leukemia deaths among irradiated patients, almost treble that
expected from national rates. Leukemia mortality was not increased among
unirradiated patients. Among those irradiated, the ratio of observed to
expected deaths for leukemia other than chronic lymphocytic leukemia was
greatest in the
period 1-5 years after the first treatment (ratio = 11.01, 95% confidence 5.26-20.98) and decreased to 1.87 (95% confidence interval
0.94-3.36) in the 25+ year period."

3) Dr. John Gofman, M.D. Ph.D, Egan O'Connor, ed. Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart
Disease: Dose-Response Studies with Physicians per 100,000 Population,
CNR Book Division, 1999.
* an Introductory chapter will be provided.

Using the number of physicians per 100,000 people in the nine census regions Dr. Gofman has demonstrated strong support for medical irradiation as "a highly important cause (probably the principal cause)
of cancer mortality in the United States during the Twentieth Century."

In his monograph, Dr. Gofman uses a 1988 and 1993 UNSCEAR (United National Committee on the Effects of Atomic Radiation) report to support
his physician- per-population method. The report states "...a good correlation was shown to exist between the number of x-ray examinations
per unit of population and the number of physicians per unit of population."

The percentages of the death-rates from all cancer caused by medical
radiation (i.e., the percentage would be absent if medical radiation were absent): females 50% , 1988; males 74%, 1988.

*4) Knox, E.G., A.M. Stewart,et al. Prenatal Irradiation and Childhood Cancer. Journal of The Society for Radiological Protection. 1987; 7(4).
Population: 14,759 geographically matched and birth-date- matched case/control pairs of children who died of cancer in England, Wales and
Scotland.
The pre-natal radiation relative risk of childhood cancer between

the
ages of 4 and 7 years is 2.11.
Time span: From 1950-79 about 7 percent of all childhood cancers, and 8
percent of those with onset between the ages of 4 and 7 years were caused by x-ray examinations.
Disease end point: Death

*5) Population: 50,000 female breast cancer patients. There was doubling
of lung cancer risk for those who chose radiation therapy versus other
methods of treatment. No dose or delivery information. Treatment was
from 1973-1986. (WSJ, May 14, 1993). Unfortunately, we could not find
the published study referenced in the Journal article.

6) Gofman, M.D., Ph.D, John W. PREVENTING BREAST CANCER: The story of a
Major, Proven, Preventable Cause of This Disease. 1996.
The author of this 450 page review of breast cancer studies concludes
that about three-quarters of recent and current breast cancer incidence
is caused by earlier exposure to ionizing radiation, primarily from
medical procedures (x-rays). For a complete list of references and the
complete book please see
http://www.ratical.org/radiation/CNR/PBC/contents.html.

Cell Studies

*1) Waldren, C, et al. "Measurement of low levels of x-ray mutagenesis
in relation to human disease." Proc. Natl. Acad. Sci. USA 1986. 83.

Mammalian cells used. Caffeine synergism found to double the mutagenic
yield of x-rays on certain cell components. X rays create a high level (about 94%) of complex genetic lesions. Complex lesions are harder to
repair and can lead to many somatic cell disease endpoints including cancer. Additionally, at lower doses there is a higher mutational efficiency than at higher doses; this observation runs counter to expected results.

Evidence for carcinogenicity of NEUTRONS

Cell
*1) Ponnaiya, M. N. et al. "Induction of Chromosomal Instability in Human Mammary Cells by Neutrons and Gamma Rays". Radiation Research 147,
1997, 288-294.
Cells: human mammary cells irradiated with 0.43 MeV neutrons
Result: Neutron irradiated cells showed cell aberrations greater than controls consistently between 5 to 40 population doublings post irradiation.

*2) Harper, K., et al. "Delayed appearance of radiation-induced mutations at the Hprt locus in murine hemopoietic cells". Experimental
Hematology 25: 263-269 (1997)
Mouse bone marrow cells irradiated with Californium-252. Note that the
researchers also performed this experiment on mouse cells with no spontaneous incidence of leukemia or particular susceptibility to radiation-induced leukemia. The result was a 2-3 fold increase in mutations 14-15 cell divisions after neutron irradiation. (please also note much the same conclusions are shown for x-rays in this study)

Conclusions: Following x- and neutron radiation of cells researchers found an increase of radiation-induced genomic instability in

descendents of these cells. The type of instability created may contribute in the accumulation of mutations necessary for tumor progression. The authors conclude by saying "The causal link between
ionizing radiation and cancers has long been established (ref. Given), although little is know about the mechanisms involved."

* On this topic, see also an overview by Prof. Eric Wright "Radiation-induced genomic instability: a brief overview" given at a symposium in 1999

Evidence for carcinogenicity of GAMMA RAYS

Human

*1) Wing, S. et al. "A Reevaluation of Cancer Incidence Near the Three Mile Island Nuclear Plant: The Collision of Evidence and Assumptions". Environmental Health Perspectives. 105 (1). 1997.
Population: General public exposed to external radiation from the Three
Mile Island accident in 1979 in the path of the released radiation plumes. Estimated dose by use of cytogenetic analysis was 60-90 rads.
Endpoint: cancer incidence
Results: increases of two to ten times were seen in leukemia, lung cancer and all cancers.

*2) Wing, PhD et al. "Mortality Among Workers at Oak Ridge National Laboratory: Evidence of Radiation Effects in Follow-up Through 1984."
JAMA 265 (11).
Population: White male employees of Oak Ridge National Laboratory, A
Department of Energy facility in Tennessee.
Endpoint: all causes of death
Conclusions: Leukemia deaths were 63% higher than expected

*3) Gardner, M. J. et al. "Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West
Cumbria". BMJ. 300. 423-429. 1990.
Population: Children who were stricken with leukemia-lymphoma in the
West Cumbria Health district, near the Sellafield nuclear reprocessing
plant.
Endpoint: leukemia-lymphoma cases
Conclusions: The relative risk of leukemia/lymphoma among children with
fathers working at Sellafield Nuclear Facility ranged from 2.44 to
6.42. "The raised incidence of leukemia, particularly , and
non-Hodgkin's lymphoma among children near Sellafield was associated
with paternal employment and recorded external dose of whole body
penetrating radiation during work at the plant before conception."

--See also Viel, JF. "Incidence of Leukaemia in Young People Around the
La Hague Nuclear Waste Reprocessing Plant: A Sensitivity Analysis".
Statistics in Medicine. 14: 2459-2472 (1995).
This study finds an association between childhood leukemia (among residents) and the La Hauge reprocessing plant in France.

*4) Kneale, G.W., A.M. Stewart. "Childhood Cancers in the UK and their Relation to Background Radiation" in Radiation and Health. Ed. By R. Russell Jones and R. Southwood. 1987. John Wiley & Sons, Ltd.
Population: UK Children
Endpoint: Cancer deaths
Conclusion: The study concludes that the effects of terrestrial gamma radiation is stronger than prenatal x-rays. The effect is even more pronounced when combined with other sources of background

radiation
including weapons testing, emissions from nuclear power and other nuclear facilities, etc. The researchers conclude that external penetrating radiation is the principle causes of childhood cancer, causing 80% of all cancer deaths before 16 years of age.

*5) National Economic Council. Occupational Illness Compensation for Department of Energy Contractor Personnel; Report of Task Group I DRAFT.
January 2000.
*6) Alvarez, R. "The Risks of Making Nuclear Weapons: A Review of the Health and Mortality Experience of U.S. Department of Energy Workers."
For The Government Accountability Project. January 2000.
Two synopses, both culling information from studies investigating the
link between cancer incidence and ionizing radiation exposure at United
States weapons fabrication facilities run by the Department of Energy.
From Alvarez "All told, workers at fourteen DOE facilities were found to
have increased risks of dying from various cancers and non malignant
diseases."

Cell

*1) Morgan, W. F. et al. "REVIEW: Genomic Instability Induced by Ionizing Radiation". Radiation Research 146, 247-258 (1996).
For a good synthesis of ionizing radiation genomic instability studies, see (Morgan, et al. 1996).
One conclusion: "The loss of stability of the genome is becoming accepted as one of the most important aspects of carcinogenesis, and the
numerous genetic changes associated with the cancer cell implicate

genomic stability as contributing to the neoplastic phenotype.

Many studies summarized in this publication show genomic instability
created by neutrons, x-rays and gamma rays.

An * indicates that a copy of this study will be provided

Thank You,

Cindy Folkers
Energy Future Project Coordinator

Enclosures by FEDEX overnight.