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Carol Langley



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

December 21, 1983

Carol Langley files 1/16

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OFFICE OF RESEARCH AND DEVELOPMENT

SUBJECT: Review of the Gilbert et al. Study of Wood Treaters in Hawaii

FROM: Herman J. Gibb
Epidemiologist
Carcinogen Assessment Group (RD-689)

TO: Amy Rispin
Chief, Science Integration Staff
Hazard Evaluation Division (TS-769)

THRU: Robert E. McGaughy *R.E. McGaughy* December 27, 1983
Acting Technical Director
Carcinogen Assessment Group (RD-689)

In response to your request to review the Gilbert et al. epidemiologic study of wood treaters in Hawaii, I have prepared the attached. This review was intended to examine the results of the study with regard to arsenic exposure and is being incorporated in the Office of Health and Environmental Assessment's document on inorganic arsenic due to be released in early 1984. David Bayliss, in a memo of September 16, 1983 to the Carcinogen Assessment Group (CAG) dioxin file, reviewed the study with regard to the wood treaters' potential exposure to dioxin which was assumed to contaminate the pentachlorophenol. A copy of David's memo is attached along with a copy of a cover memo from Charles Ris, Acting Executive Director of CAG, which forwarded David's memo to the Office of Solid Waste.

Regardless of the preservative, however, the study was unlikely to have detected an excess risk of cancer associated with any of the preservatives to which the workers were exposed. The study consisted of two parts--a cohort-comparison study and a historical prospective study. The cohort-comparison study of a cohort which consisted primarily of current workers was an inappropriate approach to assessing whether a cancer risk existed among the wood treaters. There is a good likelihood that persons who develop cancer while working have either died or left employment. Those with cancer who are still alive may not agree to an examination because of the debilitating nature of the disease. In the historical prospective study, the sample size was simply too small and the follow-up was probably not long enough to have detected an excess risk of cancer.

Attachment

cc: David Bayliss

Gilbert et al. (1983)

Gilbert et al. (1983) studied a group of 182 workers in Hawaii exposed for at least 3 months during the period 1960-1981 to the wood-treating chemicals, chromated-copper-arsenate (CCA), pentachlorophenol (penta) tributyl tin oxide (TBT0) and lindane. The study was divided into two parts (1) a cohort comparison study of 88 workers and 61 controls and (2) a historic prospective study which consisted of a morbidity and a mortality analysis of the entire cohort.

In the cohort comparison study, 61 controls were matched on the basis of age, sex, race, level of physical activity, and weight to 88 wood treatment workers who were "qualified and agreed to participate in the study." Controls were recruited from among the membership of carpenters', ironworkers', masons', plumbers', and stevedores' unions and from the names of friends and relatives referred to the study by participating members of the occupational cohort. Fourteen of the controls were reported to be carpenters and 13 of them had had exposure to either CCA or penta or both. Their urine arsenic levels, however, were reported not to differ significantly from that of other controls. The exposed group and the control group were each given a comprehensive health examination consisting of a questionnaire and clinical and laboratory tests including analysis of a urine sample for penta, arsenic, copper, chromium, and tin levels. Only penta was found to be significantly elevated in the urine of the exposed group over that of the controls. The authors reported that there were no "clinically significant" differences between the exposed group and the controls. No significant differences were found between the wood treaters and controls with respect to educational level, smoking history, or alcohol consumption.

The historical prospective study identified three cases of cancer, one by means of the questionnaire in the cross-sectional study and the other two by means of the Hawaii Tumor Registry. One of the cancer cases was a bladder cancer case, the other two were colorectal cancer. For the mortality analysis the vital status of 125 of the 182 workers (69%) was able to be determined. Of these 125, six deaths occurred, five from cardiovascular disease, the other from an unknown cause. The authors calculated that eight deaths would have occurred in this group, three of which would have been from cancer. The authors did not state the basis of the expected number of cancer deaths.

There are limitations in the study design and sample size of this study which make the results with regard to the evaluation of a cancer risk among the wood treaters inconclusive. A cohort comparison study on the basis of a single medical examination is an inappropriate approach to determine if a cancer risk exists in the wood treater group particularly when the group consist primarily of persons who are currently employed as wood treaters (60 of 88 were current employees). Most persons who have developed cancer will either have died or left the work force. In addition, the sample size (88 current or former wood treaters and 61 controls) would have been too small to detect an excess cancer risk. Also, it should be noted that the inclusion in the controls of 13 carpenters who had been exposed to arsenic-treated wood certainly presents a potential bias despite the fact that the authors claimed that the levels of arsenic in the urine of these 13 were not significantly different from those in other controls. In this regard it should be noted that no effort had apparently been made to restrict seafood intake, which will usually elevate urine arsenic levels, prior to collection of the urine samples. The mean level of urinary arsenic in both the study

group and in the controls was significantly ($P < 0.01$) higher than what the authors reported would be a normal level.

The historic prospective study also had limitations. Again, the sample size was simply too small to adequately determine whether an excess risk of cancer existed in the study cohort. Only 125 were included in the mortality study and only 182 were included in the morbidity study. Arsenic exposure via inhalation and ingestion is known to be associated with lung and nonmelanoma skin cancer, respectively. Nonmelanoma skin cancer is rarely fatal and thus, an excess risk of skin cancer would not have been detected in such a small mortality study. The Hawaii Tumor Registry which was used to identify cancer cases in the study population does not even report nonmelanoma skin cancer.

There is also a question of whether the authors had sufficiently allowed for a cancer latency period in their study. The authors did not indicate the length of follow-up of the cohort members. Some indication is provided, however, in the data reported by the authors on the length of employment of the 88 workers in the study cohort of the cohort comparison study. These workers were part of the larger incidence and mortality studies. Of the 88 workers, 60 had worked 10 years or less and 80 had worked 15 years or less at the time of the physical examination in 1981. Twenty-two of the study cohort in the cohort comparison study were former employees. At the minimum, however, assuming that the workers had had no breaks in employment, 58 of 125 (46%) in the mortality study would have been followed for only 15 years or less and 38 of 125 (30%) would have been followed for only 10 years or less. In the morbidity study, if again we assume no breaks in employment of the workers, 58 of 182 (32%) would have been followed for only 15 years or

less and 38 of 182 (21%) would have been followed for only

In conclusion this study is simply inadequate to conclude
excess risk of cancer exists in the wood treater population

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 16 1983

OFFICE OF
RESEARCH AND DEVELOPMENT

SUBJECT: 1981 Hawaii Epidemiology Study Submitted to the Office of Solid Waste by Reichhold and Vulcan Company's for Section 3001 Dioxin Docket

FROM: Charles Ris
Acting Executive Director
Carcinogen Assessment Group

TO: Judy Bellin
Office of Solid Waste

You recently asked us to take a look at the referenced study and evaluate its impact on the pending Section 3001 listing decision for dioxin.

The Hawaii study concerns exposures to pentachlorophenol and other wood preserving chemicals; The Office of Solid Waste (OSW) listing action is dealing with all known isomers of dioxin. The common area in this seeming mismatch of chemicals is that pentachlorophenol usually contains impurities including hexachlorodibenzo-p-dioxin and 2 other isomers, but not the 2,3,7,8 isomer.

We have evaluated the epidemiology study for the cancer aspects (see attached) and feel that the findings cannot be construed to support a negative finding for a cancer effect because of study limitations, the most important of which are: first, that a cross-sectional study design is not a suitable method for detecting a cancer effect, i.e., persons with cancer who are currently employed are not likely to be identified in a cross-sectional study as having cancer; secondly, the historical prospective study is not supportive of either a positive or negative finding for cancer again because the sample size and insufficient latent period following the onset of exposure did not allow the detection of a cancer effect.

The 1981 study, while seemingly showing no elevated risk of cancer, is not an adequate study of the exposed population such that the findings can be equally weighed with other dioxin related epidemiology and animal studies.

Attachment

cc: David Bayliss
Charli Hiremath
Debdas Mukerjee