

CHAPTER 7

MALIGNANCY ASSESSMENT

INTRODUCTION

Background

Cancer is a major suspect disease following exposure to chlorophenols, phenoxy herbicides, and dioxin. Both systemic cancer and skin cancer are key focal points of this study. At present, there is no scientific consensus on the dioxin-cancer question. There is, however, concern that some malignancies including soft tissue sarcoma (STS) and non-Hodgkin's lymphoma (NHL) may be associated with dioxin exposure.

Traditional difficulties in extrapolating animal data to humans and interspecies variability have limited the direct applicability of much of the experimental work. Other major challenges have included difficulties in the ability to control or characterize bias; selection of suitable controls or reference groups; quality and quantity of exposure; misclassification of exposure; confounding exposure to known injurious chemicals; sample size and statistical power; number and selection of relevant risk factors; and the lack of clearly defined clinical endpoints for study.

Numerous animal studies have been conducted to delineate the role of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on tumor initiation, tumor promotion, mutagenesis, cocarcinogenesis, and deoxyribonucleic acid (DNA) reactivity. The consensus of most research is that TCDD is only weakly mutagenic, does not covalently bind to DNA or cause it to initiate repair synthesis, but behaves as a strong tumor promoter in already initiated cells (1). Recent animal studies have supported the theory that TCDD-induced response is mediated by a nongenotoxic mechanism. TCDD, binding to the Ah receptor, appears to alter cellular regulatory mechanisms resulting in enhanced cellular proliferation (2-6).

The oncogenic response to TCDD in animals has been shown repeatedly to depend upon the age, sex, and strain of species, as well as the dose and route of administration (7, 8, 9). In the presence of a strong carcinogen, TCDD induced skin papillomas in homozygous hairless mice but not in the heterozygous strain. This clearly supports the promoter role of TCDD, a nongenetic mechanism judged to be related to receptor binding (10).

Studies in rodents produced hepatocellular carcinomas, squamous cell carcinomas of the oropharynx and lung, and follicular cell thyroid adenomas (11, 12, 13). TCDD has been shown to affect the action of estrogen in a number of tissues, possibly leading to carcinogenesis. In rats, TCDD has been shown to promote liver cancer but to inhibit uterine and mammary tumors due to interference with estrogen activity (14, 15). TCDD also exhibits antiestrogenic activity (16, 17, 18) in human cancer cells.

Based upon these and other studies, the International Agency for Research on Cancer designated TCDD as carcinogenic in 1982. There are insufficient data to implicate 2,4-D and 2,4,5-T as carcinogens.

In a series of publications beginning in 1974, commonly known as the "Swedish studies," extensive inquiry was made into occupational cancer following exposure to a variety of herbicides. Four related efforts (19-22) using Swedish railroad workers found an increased cancer incidence associated with non-TCDD containing herbicides. However, a review of these studies by other investigators suggested cancer promotion following phenoxy acid exposure (23).

Prompted by a slight increase in STS in the railroad workers and clinical experience with a case series of STS, Hardell and coworkers launched an extensive second round of studies (24-32). These efforts showed statistically significant increased risks for STS, Hodgkin's Disease (HD), and NHL. For exposure to phenoxy acids alone, the risk ratio ranged from 5.3 to 6.8 for STS in northern and southern Sweden, respectively, while a range of 3.3 to 6.6 was noted for exposure to chlorophenol alone. For malignant lymphoma (HD plus NHL), risk ratios of 8.4 and 4.8 were respectively demonstrated for chlorophenol and phenoxy acid exposures. An association of nasal and nasopharyngeal cancer to chlorophenol exposure (risk ratio, 6.7) was also detected (30), but other specifically focused studies of primary liver cancer and colon cancer were negative with respect to phenoxy acid or chlorophenol exposure (29, 31). The colon cancer study was conducted specifically to demonstrate a lack of respondent bias to "validate" previous questionnaire and interview methods used in the STS studies.

From the outset, the Swedish studies have been criticized on methodologic issues (33, 34, 35), prompting the primary authors, Axelson and Hardell, to respond with clarifications, new calculations, amplifying studies on additional cohorts, and studies on other cancers (29, 32, 36-38). The chief criticisms centered upon possible respondent and observational biases, selection of controls, confounding exposures, and the degree of true exposure to phenoxy acids and chlorophenols. The authors answered these criticisms within the inherent constraints of the case-control methodology. Their efforts have been characterized as careful, clever, and properly stated, and have received favorable reviews (39, 40).

The principal investigators of the Swedish studies have published reports of more recent studies in an attempt to clarify and strengthen their earlier results mentioned above (41, 42). Employing a case-control design and including only cases confirmed by histopathologic examination, they compared 55 cases of STS with 220 living and 110 deceased population-based controls. To reduce the potential impact of exposure recall bias in patients with cancer, a second control group from the same tumor Registry was created which included 190 individuals with forms of cancer other than STS, malignant lymphoma, or nasopharyngeal cancer. Exposure to phenoxyacetic acids was determined by a questionnaire that was followed up by direct telephone contact by trained interviewers blinded to the disease status of participants. The authors concluded that the relative risk for STS in the exposed group was 3.3 (95% C.I.: [1.4,8.1]) when compared to the population-based control group and 2.2 (95% C.I.: [0.9,5.3]) relative to the controls with other forms of cancer.

Though the results of this study tend to confirm the authors' previous observations, the relative risk for developing STS was considerably lower than that found in the earlier studies. Furthermore, when compared with the control group with other forms of cancer, the relative risk was not statistically significant. In contrast to previous studies, the authors found no increased risk for STS in association with chlorophenol exposure. Finally, the authors

acknowledge that a principal limitation in all the occupational studies to date has been the difficulty in determining whether risk is associated with exposure to phenoxyacetic acids or to contaminants such as 2,3,7,8-TCDD. In their most recent study, the authors cited evidence that the increased risk of STS may in fact be due to other higher chlorinated isomers of dioxin (42).

Four small industrial mortality studies were conducted in the late 1970's and early 1980's (43-46). National Institute for Occupational Safety and Health investigators pooled the data from these studies and noted that 3 of the 105 deaths (2.9%) in these studies were due to STS, as contrasted to an expected 0.07 percent in the U.S. general population (47). This study was criticized for the addition of possibly noncomparable industrial cohorts and the lack of histologic confirmation of the STS cases. A subsequent case report added another STS case to the industrial studies (48), and two other reports revealed three unrelated STS cases also arising from the industrial sector (49, 50). However, upon closer inspection, only two of the first four cases were confirmed as STS by an independent histologic review (51). Other reviews of the seven total cases were noteworthy: there was poor agreement on the histologic subtype of the soft tissue tumors, and, because of a feature of the International Classification of Diseases, 9th Revision, (ICD-9) system, wherein organ-specific sarcomas are coded separately from soft and connective tissue tumors (ICD code 171), death certificate-based studies underascertain STS by approximately 40 percent (51, 52). (This latter problem did not affect the Swedish studies.) Two studies of workers from Dow Chemical's Midland facility have indicated slightly increased levels of some cancers (primarily soft tissue), but none of statistical significance (53, 54). A study of workers exposed during a 1953 accident at a BASF plant in Germany also showed no statistically significant increases in cancers, but this study may have suffered from an insufficient cohort size (55).

Other cancer studies throughout the world showed mixed support for the Swedish findings. An Italian case-control effort (56) showed a weak association between ovarian mesothelial tumors and herbicide exposure, whereas a Finnish study of a small number of pesticide sprayers understandably did not detect any cases of STS or malignant lymphomas (ML) (57). A study of more than 4,000 Danish phenoxy herbicide workers noted five STS cases (versus 1.8 expected) and seven ML cases (versus 5.4 expected) (58). The author concluded that the STS observation supported the Swedish work and that the ML data did not.

One New Zealand case-control study showed a nonsignificant relative risk of 1.3 for STS among occupations consistent with phenoxy herbicide exposure (59), although a risk of 7.2 was noted for STS and potential chlorophenol exposure in tanneries.

A related cancer registry-based, case-control study revealed significant excesses of agricultural and forestry occupations from ML cases and multiple myeloma cases (odds ratio 1.25) (60). A recent (1987) expanded version of this study found no increase in risk of NHL and no trend toward increasing risk with increasing duration and intensity of exposure (61). In a similar but larger cancer registry study in Sweden, there was no increased risk of STS (relative risk: 0.9) in agricultural or forestry workers as contrasted to other industrial workers (62). Furthermore, the STS risk was constant over time in spite of an increased

usage of phenoxy acid herbicides from 1947 to 1970. This Swedish study did not confirm or show a trend consistent with the earlier Hardell studies.

Other recent occupational epidemiologic studies have focused on the incidence of lymphoma in agricultural workers. Using a similar protocol, other Swedish investigators expanded a previous study cited above (62) to include an analysis of HD and NHL (63). In the total study cohort, which was made up of 354,620 men employed in various forestry and agriculture occupations, no increase in the relative risk for NHL was found. Statistically significant elevations in relative risk for HD were found in two subcohorts, but further analysis failed to support an association with herbicide exposure. Of the 15 cases of HD in silviculture workers, 8 occurred in managers or administrators.

The principal limitation of uncertain exposure in this and other studies (64, 65) was addressed in a recent mortality study of 322 Dow Chemical employees who met probable or definite criteria for chloracne, an undisputed marker of high level exposure to dioxins and related compounds (66). Thirty-three deaths occurred in the study cohort versus 39.5 expected. None of the deaths was related to the suspect cancers listed above.

A recent U.S. case-control study from the Kansas cancer registry has provided partial support for Hardell's observations (67). The Kansas study was very similar in methodology to the early Swedish studies and tried to avoid bias and misclassification. An overall relative risk of 1.6 was found for NHL in men exposed to herbicides, particularly 2,4-D. As the frequency of herbicide exposure increased to more than 20 days per year, the relative risk of NHL increased to 6.0 as compared to nonfarmers. For herbicide applicators, the relative risk for NHL was 8.0. A simultaneously published review of the Kansas work noted that this should shift scientific concern from STS to NHL (68). A population-based, case-control study of STS and NHL in western Washington found no overall increased risk of these diseases associated with an occupational history of exposure to chlorophenols or phenoxy herbicides (69). However, risks of NHL were significantly elevated in the specific occupational categories of farmers, forestry herbicide applicators, and individuals potentially exposed to phenoxy herbicides in any occupation for 15 years or more. An increased risk of NHL was also noted among those with occupational exposure to insecticides, organic solvents, lead, and welding fumes.

Several studies of Vietnam veterans have attempted to determine whether veterans have experienced excessive mortality, particularly from cancer (70-77). Most of the studies used proportionate mortality ratio (PMR) methodology and equated Vietnam service with potential exposure to Agent Orange, a procedure of considerable imprecision (misclassification). These exposure allocation difficulties, coupled with the inherent methodological weaknesses of the PMR technique, have minimized the contribution of these studies to the clarification of the cancer issue.

Several important studies of the incidence of cancer in Vietnam veterans have recently been published, although, with the exception of the Air Force Health Study (AFHS), they have not been designed to relate the incidence of cancer to herbicide exposure. The mortality component of the Vietnam Experience Study by the U.S. Centers for Disease Control (CDC) found the overall mortality from cancer to be similar in Vietnam and non-Vietnam veterans

(78). In a cohort mortality study of Army and Marine Corps veterans (79), service in Vietnam was associated with a slightly elevated proportionate mortality ratio for all causes of cancer and, for cancers at specific sites, an increase in mortality rates due to lung cancer and NHL. Neither Army nor Marine veterans had an apparent increase in risk for STS.

In the latest report of the third examination cycle of the AFHS, the frequency of systemic cancer for Ranch Hands and Comparisons was similar (80). Ranch Hand participants continued to have a greater incidence of basal cell skin cancer. Mortality studies have shown no significant differences between the Ranch Hand and Comparison cohorts (81).

To date, almost all of the studies of veterans were negative for aggregate cancer associations. As an example of the veteran studies, the Australian retrospective cohort mortality effort revealed an overall relative mortality ratio of 0.99, an overall cancer mortality ratio of 0.95, and nonsignificant statistical differences for STS, NHL, and HD (73). Two more recent case-control studies found no evidence for an increased risk of STS in association with military service in Vietnam (82, 83).

The recently released (though not yet published) Selected Cancers Study (SCS) of the U.S. CDC focused more specifically on the incidence in Vietnam veterans of the NHL, STS, HD, nasal and nasopharyngeal carcinoma, and primary liver cancer. The case-control design of the study was selected as one that requires fewer subjects than a cohort study and as the only feasible method for studying rare cancers with a long latency period. The SCS was designed to compare the risk of specific cancers among Vietnam veterans relative to that in men with no military service in Vietnam. This study was based on diagnoses of malignant disease reported by eight tumor registries in the United States, providing surveillance of 10 percent of the total U.S. population. The comparison group was drawn from random telephone interviews and included men of the same age who did not have any of the six cancers under study. Interviews were based on a standardized questionnaire with high participation in both case (87%) and control (85%) groups. The relative risk of the specific cancers occurring in association with military service in Vietnam was determined by an odds ratio (OR).

Results of the SCS defined a statistically significant ($p=0.01$) increase in relative risk ($RR=1.47$; 95% C.I.: [1.09,1.97]) for the development of NHL in Vietnam versus non-Vietnam veterans. Further analysis failed to reveal any significant increase in risk related to age at time of service, rank, or job description (combat, combat support, or support). Navy and Marine veterans were at a slightly greater risk but the difference was not statistically significant. Pertinent to the current report, there was no evidence that the increased risk of NHL was associated with factors thought to indicate an increased likelihood of herbicide exposure. Furthermore, Vietnam veterans who served in III Corps (the combat zone with the heaviest use of Agent Orange) were at slightly lower risk than veterans serving in other regions.

More detailed summaries of the pertinent scientific literature for the malignancy assessment can be found in the report of the previous analyses of the 1987 examination data (80).

Summary of Previous Analyses of the 1987 Examination Data

The unadjusted analysis of all verified neoplasms indicated that the proportion of Ranch Hands with neoplasms was significantly greater than that of the Comparisons. After including suspected neoplasms with verified neoplasms, the Ranch Hand proportion was marginally greater than the Comparison proportion. The majority of malignant neoplasms observed in the Ranch Hands were basal cell carcinomas, a nonlife-threatening form of skin cancer. When the analysis was performed only on skin neoplasms for non-Black participants, significantly more Ranch Hands had skin neoplasms than did the Comparisons for both the verified and the verified and suspected diagnoses. A significantly greater proportion of Ranch Hands had verified malignant skin neoplasms than did the Comparisons. Given the presence of a neoplasm, a marginally significant higher proportion of Ranch Hands had skin neoplasms than did the Comparisons.

In the unadjusted analyses of verified basal cell carcinoma, a marginally significant group difference was found. The unadjusted analysis of the verified and suspected basal cell carcinomas was not significant. After adjustment for covariates, the group contrast was statistically significant for verified basal cell carcinoma and marginally significant for the verified and suspected diagnoses. Ranch Hands and Comparisons differed significantly on the frequency of participants with zero, one, or multiple verified basal cell carcinomas. Also, the Ranch Hands had a significantly higher percentage of participants with multiple verified basal cell carcinomas than did the Comparisons.

Sun exposure-related malignant skin neoplasms also exhibited group differences. (Approximately 90 percent of the participants with sun exposure-related malignant neoplasms had basal cell carcinomas.) For the unadjusted analysis, the group contrast was significant for the verified diagnoses and marginally significant for the combination of verified and suspected sun exposure-related malignant skin neoplasms. For the adjusted analysis of these neoplasms, the Ranch Hands and Comparisons differed significantly for both the verified and combined diagnoses.

No significant group differences were found in the analyses of systemic neoplasms by number, behavior (malignant, benign, uncertain behavior, or unspecified nature), or by location and site. Thus, the increase in overall malignancy was due to elevated relative risks for skin cancer (basal cell carcinoma). Also, given the presence of any systemic neoplasm, Ranch Hands and Comparisons did not differ significantly for malignant systemic neoplasms. The number of STS and NHL was comparable in the two groups. For the 1985 examination, one Ranch Hand and one Comparison had verified STS (fibrous histiocytoma and fibrosarcoma, respectively). The Ranch Hand was not part of the 1987 study because he died; the Comparison with the fibrosarcoma was part of the 1987 examination. At the 1985 examination, one Ranch Hand was classified as having a suspected leukemia, HD, or NHL. He was diagnosed as a verified leukemia by the time of the 1987 examination. At the 1987 examination, there was one verified case of NHL in a Ranch Hand.

The fixed size of the Ranch Hand cohort limited the ability of the study to detect group differences for the rare forms of cancer (particularly STS and NHL). The study had virtually no statistical power to detect low to moderate group differences for these malignancies. The study had good power to detect relative risks of 2.0 or more with respect to disease occurring

at prevalences of at least 5 percent in the Comparison group, such as basal cell carcinoma and all systemic cancers combined.

Parameters for the Malignancy Assessment

Dependent Variables

The malignancy assessment was based on lifetime incidence of neoplasms exclusive of the neoplasms occurring before the Southeast Asia (SEA) tours of duty. Information on the occurrence of neoplasms was captured in the health questionnaires and the physical examinations at Baseline (1982) and the 1985 and 1987 studies and was coded according to conventions in the International Classification of Diseases, 9th Edition, Clinical Modification manual. Information on neoplasms from the questionnaire and the physical examination were combined to form a lifetime incidence of neoplasms for each participant.

The term "neoplasm" refers to any new growth that may or may not be malignant. Malignant neoplasms are those neoplasms capable of invasion and metastasis. Malignant and benign neoplasms, carcinomas in situ, and neoplasms of uncertain behavior or unspecified nature as well as skin and systemic neoplasms were studied. Systemic neoplasm was used to denote a nonskin neoplasm.

The malignancy assessment was based on the number of participants in the 1987 study with serum dioxin assays, and not on the number of neoplasms. A participant was considered to have an adverse health condition for the malignancy assessment if he had one or more neoplasms.

Questionnaire and Physical Examination Data

During the 1987 health interview, each study participant was asked a series of questions on the incidence of cancer since the date of his last health interview. Participants who were new to the AFHS also completed the Baseline health questionnaire. The self-reported conditions were verified by medical record review. The verification status of each self-reported neoplasm was classified as (1) verified (supported by medical record), (2) nonverifiable (not supported by medical record), or (3) pending (medical record not yet provided). The reported neoplasms for which the verification status is pending were called suspected neoplasms. Only data on verified or suspected neoplasms were used in the malignancy assessment. All reported neoplasms in the Ranch Hands were verified. Suspected neoplasms only occurred among the Comparisons.

Some possible neoplastic conditions were discovered by the physicians at the physical examination. Contingent upon participant authorization, suspicious skin lesions were biopsied, and the pathology was determined; however, no invasive procedures were used to detect systemic neoplasms. For some suspicious skin lesions and suspected systemic neoplasms, the verification process had not been completed by the time of the data analysis. Both the verified and suspected (verification not completed) neoplasms from the physical examination were used in the analysis. This was deemed necessary in order to describe the complete neoplasm findings, recognizing that confirmation of all suspected cases was difficult.

Skin Neoplasms

The analysis of skin neoplasms for the malignancy assessment was divided into four sets. Each set was analyzed for an association with initial dioxin, with current dioxin and time since tour, and with categorized current dioxin. The first two types of analyses (i.e., Ranch Hand-only analyses) used verified skin neoplasms only because there were no unconfirmed cases. For the analysis using categorized current dioxin, verified skin neoplasms were analyzed as well as the combination of verified and suspected neoplasms, wherever possible.

Analysis set 1 consisted of analyses of skin neoplasms by behavior. Four behavior types were examined: (1) all skin neoplasms, (2) malignant neoplasms only, (3) benign neoplasms only, and (4) neoplasms of uncertain behavior or unspecified nature.

Analysis set 2 consisted of analyses of malignant skin neoplasms by cell type. Four types were analyzed: (1) basal cell carcinoma, (2) sun exposure-related malignant skin neoplasms (basal cell carcinoma, squamous cell carcinoma, melanoma, and malignant epithelial neoplasms not otherwise specified [NOS]), (3) melanoma, and (4) squamous cell carcinoma. Analyses of basal cell carcinoma, melanoma, and sun exposure-related malignant skin neoplasms were conducted for all sites combined and by location/site. Five locations/sites were examined: (1) ear, face, head, and neck; (2) trunk; (3) upper extremities; (4) lower extremities; and (5) other sites (including sites NOS). Squamous cell carcinoma was analyzed for all sites combined.

Analysis set 3 consisted of analyses of basal cell carcinoma and sun exposure-related malignant skin neoplasms by occupation. For both groups of neoplasms, the analyses were performed on the number of participants with neoplasms on the ear, face, head, and neck, as compared to the number of participants with no neoplasms. These analyses were repeated using all other sites combined.

In addition, an analysis of participants having one or more basal cell carcinomas versus no basal cell carcinomas was conducted.

Because there were relatively few Blacks in this study (n=32 for the minimal assumption; n=38 for the maximal assumption; and n=80 for the categorized current dioxin analyses), and since Black participants exhibited only benign skin neoplasms, most of the subsequent analyses were limited to non-Blacks. However, both Blacks and non-Blacks were combined in the analysis of benign skin neoplasms. No participants were excluded for medical reasons from the analysis of these variables.

Systemic Neoplasms

The systemic neoplasms were analyzed by behavior and body site. As with skin neoplasms, each analysis was conducted using verified data and, when possible, also verified and suspected neoplasms. The analysis of the systemic neoplasms was divided into two sets, described below.

Analysis set 1 consisted of analyses of systemic neoplasms by behavior. Four behavior types were examined: (1) all systemic neoplasms, (2) malignant neoplasms, (3) benign neoplasms, and (4) neoplasms of uncertain behavior or unspecified nature.

Analysis set 2 consisted of analyses of malignant systemic neoplasms by site: (1) ear, head, face, and neck; (2) oral cavity, pharynx, and larynx; (3) brain; (4) thymus and mediastinum; (5) thyroid; (6) bronchus and lung; (7) colon and rectum; (8) kidney and bladder; (9) prostate; (10) testicles; (11) ill-defined sites; (12) carcinoma in situ of penis; and (13) carcinoma in situ of other and unspecified sites.

In addition to the analyses described above, the number of participants with Hodgkin's disease, leukemia, and malignant neoplasms of lymphoid and histiocytic tissue were analyzed.

No participants were excluded for medical reasons from the analysis of these variables.

Skin and Systemic Neoplasms

All neoplasms, skin and systemic combined, were analyzed for an association with initial dioxin, with current dioxin and time since tour, and with categorized current dioxin. As in analyses of skin neoplasms only and systemic neoplasms only, the Ranch Hand-only analyses were performed using verified diagnoses. The categorized current dioxin analysis was performed using participants with a verified neoplasm and using participants with verified and suspected neoplasms.

There were no medical exclusions in the analysis of these variables.

Covariates

The emphasis on cancer was increased during the 1985 study. In particular, the interval health questionnaire was modified to collect information on each geographic location in which a participant lived for more than 12 months. Because ultraviolet light exposure has been acknowledged as the primary cause of basal cell carcinoma, this information was used to compute a cumulative sun-exposure index based on residential history. An average lifetime residential latitude was estimated by dividing the total degree-years (i.e., the sum of the product of latitude [degrees] and the number of years lived at each residence) from all residences by the total number of residential years reported on the questionnaire. In addition, detailed information on skin tannability; eye, skin, and hair color; parental ethnicity; and lifetime smoking history was obtained. This information was obtained for participants in the 1987 examination who did not attend the 1985 examination.

In the 1987 examination, the questionnaire was expanded to capture a detailed history of alcohol consumption. Baseline questions on exposure to carcinogens were repeated to collect interval data. Interval smoking patterns were also captured.

In the analysis of the 1987 examination results, 33 covariates were candidates for adjusted statistical analyses assessing basal cell carcinoma and sun exposure-related malignant skin neoplasms. Analyses of skin neoplasms were limited to non-Blacks.

Candidate covariates included age, lifetime cigarette smoking history, lifetime alcohol history, ethnic background, skin color, hair color, eye color, reaction of skin to sun exposure, the composite sun-reaction index, average lifetime residential latitude, and exposure to individual carcinogens and groups of carcinogens. For lifetime cigarette smoking history and lifetime alcohol history, the respondent's average daily smoking and average daily alcohol consumptions were estimated over his lifetime, assuming 365 packs of cigarettes equaled 1 pack-year and 365 drinks equaled 1 drink-year, respectively.

The candidate covariates for the systemic malignancy assessment were the same as those for the skin malignancy assessment with the following exceptions:

- Race was added as a candidate covariate.
- The following covariates specific to skin were deleted: ethnic background, skin color, hair color, eye color, reaction of skin to sun exposure, sun-reaction index, and average lifetime residential latitude.

Definitions and categories of candidate covariates are provided below:

- Ethnic Background: (A) English, Welsh, Scottish, or Irish; (B) Scandinavian, German, Polish, Russian, other Slavic, Jewish, or French; (C) Spanish, Italian, or Greek; (D) Mexican, American Indian, or Asian; and (E) African.
- Skin Color: dark, medium, pale, dark peach, and pale peach.
- Hair Color: black, dark brown, light brown, blonde, and red.
- Eye Color: brown, hazel, green, gray, and blue.
- Two reactions of the skin to sun exposure:
 - 1) At Least 2 Hours Sun Exposure, After First Exposure: burns painfully, burns, becomes red, and no reaction.
 - 2) After Repeated Sun Exposures: freckles with no tan, tans mildly, tans moderately, and tans deep brown.
- Composite Sun-Reaction Index: a composite variable based on two reaction of skin to sun exposure variables was defined as follows: (1) burns painfully and/or freckles with no tan, (2) burns and/or tans mildly, and (3) all other reactions.
- Average Lifetime Residential Latitude: average latitude less than 37 degrees and average greater than or equal to 37 degrees.
- Exposure to Carcinogens or Groups of Carcinogens:
 - Set 1: asbestos, ionizing radiation, industrial chemicals, herbicides, insecticides, and degreasing chemicals (yes/no for each).
 - Set 2: anthracene, arsenic, benzene, benzidine, chromates, coal tar, creosote, aminodiphenyl, chloromethyl ether, mustard gas, naphthylamine, cutting oils, trichloroethylene, ultraviolet light (not sun), and vinyl chloride (yes/no for each).

Composite Carcinogen Exposure Index: yes, if exposure to any carcinogen in set 2; no, otherwise. Self-reported information on exposure to the 15 individual carcinogens of set 2 was obtained at the physical examination. Because substantially fewer participants reported exposure to the individual carcinogens than those of the questionnaire-based items addressing the individual carcinogens in set 1, and in the interest of reducing the number of possible covariates, a composite carcinogen exposure index was constructed from the set of 15 carcinogens.

As described in the previous report on the 1987 examination study (see page 10-10, [80]), the malignancy assessment contained more than 30 candidate covariates for use in adjusted analyses of skin and/or systemic neoplasms. Because of the large number of covariates, a reduced set of candidate covariates was determined for the analyses of the skin neoplasms by examination of the dependent variable-covariate associations and a statistical screening procedure (see pages 10-44, 10-45, and Appendix Table G-2, [80]). Based on these evaluations, the covariates of age, skin reaction after at least 2 hours of sun exposure, skin reaction after repeated sun exposure, ethnic background, average lifetime residential latitude, and ionizing radiation exposure were selected as covariates to be evaluated under the stepwise modeling procedure. (Occupation was also a covariate included in the skin neoplasm analyses of the 1987 examination report [80]; however, because of its implicit strong association with dioxin, it is not used as a candidate covariate for the serum dioxin analyses.) An examination of the associations between dioxin and the individual covariates resulted in expanding the above group of six covariates to also include hair color in the stepwise modeling procedure for the serum dioxin analyses of the skin neoplasms.

Also, as documented in the 1987 examination report (see page 10-57, [80]), age, race, lifetime cigarette smoking history, and lifetime alcohol history were covariates used in the stepwise modeling procedure for the adjusted analyses of the systemic neoplasms. (Occupation was also used in the adjusted analyses; however, as noted earlier, it is not being used for the serum dioxin analysis.) Based on an examination of the associations between dioxin and individual covariates, as well as the associations between individual covariates and groups of systemic neoplasms (i.e., all systemic, malignant systemic, benign systemic neoplasms), the composite carcinogen exposure index was included with the other covariates of age, race, lifetime cigarette smoking, and lifetime alcohol history for use in the stepwise modeling procedure for the serum dioxin analyses of the systemic neoplasms.

Relation to Baseline, 1985, and 1987 Studies

Most dependent variables and covariates analyzed in the serum dioxin analyses of the malignancy data were analyzed in the 1985 and 1987 studies. Basal cell carcinoma replaced a similar analysis involving nonmelanoma malignant skin neoplasms by location and occupation. In general, the same variables were analyzed in the Baseline study, although less covariate information was captured at that time.

Statistical Methods

Chapter 4, Statistical Methods, describes the basic statistical analysis methods to be used in the malignancy assessment.

Table 7-1 summarizes the statistical analyses that were performed for the malignancy assessment. The first part of this table identifies the dependent variables and the statistical methods. This information is presented in three sections: skin neoplasms, systemic neoplasms, and skin and systemic neoplasms. Data source, data form, cutpoints, and candidate covariates are summarized at the end of the table. The second part of the table describes the candidate covariates. Abbreviations are used in the body of the table and are defined in footnotes. Table 7-2 summarizes the number of participants with missing data on specified covariates.

Appendix F contains graphic displays of relative frequencies of Ranch Hands with a specified neoplasm versus initial dioxin under the minimal and maximal assumptions and relative frequencies of Ranch Hands and Comparisons with a specified neoplasm versus current dioxin. Appendix F also presents graphics for dioxin-by-covariate interactions determined by various statistical models.

Appendix Table F-1 presents tabular displays of these dioxin-by-covariate interactions. In addition, Appendix Tables F-2 through F-5 contain listings, by group, of skin and systemic neoplasm conditions used in the analyses.

Three statistical approaches were used to examine the association between the frequency of participants with a specified neoplasm and serum dioxin levels. One model related a dependent variable to each Ranch Hand's initial dioxin value (extrapolated from current dioxin values using a first-order pharmacokinetic model). A second model related a dependent variable to each Ranch Hand's current serum dioxin value and each Ranch Hand's time since tour. The phrase "time since tour" is often referred to as "time" in discussions of these results. Both of these models were implemented under the minimal and maximal assumptions (i.e., Ranch Hands with current dioxin above 10 ppt and above 5 ppt, respectively). The third model compared the dependent variable for Ranch Hands having current dioxin values categorized as unknown, low, and high with Comparisons having background levels. The contrast of the entire Ranch Hand group with the complete Comparison group can be found in the previous report of analyses of the 1987 examination (80). All three models were implemented with and without covariate adjustment. Chapter 4 provides a more detailed discussion of the models.

RESULTS

Exposure Analysis

Questionnaire and Physical Examination Data

In the malignancy assessment of the report on the 1987 examination results, statistical analyses were performed separately for participants with a verified neoplasm only and for participants with verified and suspected neoplasms combined. For the serum dioxin report, most of the neoplasms were verified (only two participants, both Comparisons, had a suspected neoplasm that was not verified). In particular, for analyses involving only Ranch Hands (i.e., initial dioxin analyses, current dioxin and time since tour analyses), only verified neoplasms were analyzed because no Ranch Hands had a suspected neoplasm. For analyses involving both Ranch Hands and Comparisons (i.e., the categorized current dioxin

TABLE 7-1.
Statistical Analysis for the Malignancy Assessment

Dependent Variables

<u>Category</u>	<u>Location/ Site</u>	<u>Statistical Analyses</u>
Skin Neoplasms		
<u>Behavior</u>		
All	All	U:LR A:LR
Malignant	All	U:LR A:LR
Benign	All	U:LR A:LR
Uncertain Behavior or Unspecified Nature	All	U:LR,CS,FT A:LR
<u>Cell Type and Location/Site</u>		
Basal Cell Carcinoma	All Sites Combined Ear, Face, Head, and Neck Trunk Upper Extremities Lower Extremities Other Sites and NOS	U:LR,CS,FT A:LR
Sun Exposure-Related Malignant	All Sites Combined Ear, Face, Head, and Neck Trunk Upper Extremities Lower Extremities Other Sites and NOS	U:LR,CS,FT A:LR

TABLE 7-1. (Continued)
Statistical Analysis for the Malignancy Assessment

Dependent Variables

Category	Location/ Site	Statistical Analyses
Skin Neoplasms		
Melanoma	All Sites Combined Ear, Face, Head, and Neck Trunk Upper Extremities Lower Extremities Other Sites and NOS	U:LR,CS,FT A:LR
Squamous Cell Carcinoma	All Sites Combined	U:LR,CS,FT A:LR
<u>Cell Type and Location/Site by Occupation</u>		
Basal Cell Carcinoma	Ear, Face, Head, and Neck All Other Sites and NOS None	U:LR,CS,FT A:LR
Sun Exposure-Related Malignant	Ear, Face, Head, and Neck All Other Sites and NOS None	U:LR,CS,FT A:LR
Skin Neoplasms		
Multiple Basal Cell Carcinoma	All	U:LR,CS,FT A:LR
Systemic Neoplasms		
All	All	U:LR A:LR
Malignant	All	U:LR,CS,FT A:LR
Benign	All	U:LR A:LR
Uncertain Behavior or Unspecified Nature	All	U:LR,CS,FT A:LR

TABLE 7-1. (Continued)
Statistical Analysis for the Malignancy Assessment
Dependent Variables

<u>Category</u>	<u>Location/ Site</u>	<u>Statistical Analyses</u>
<u>Location/Site</u>		
Malignant	Ear, Face, Head, and Neck	U:LR,CS,FT A:LR
Malignant	Oral Cavity, Pharynx, and Larynx	U:LR,CS,FT A:LR
Malignant	Brain	U:LR,CS,FT A:LR
Malignant	Thymus and Mediastinum	U:LR,CS,FT A:LR
Malignant	Thyroid Gland	U:LR,CS,FT A:LR
Systemic Neoplasms		
Malignant	Bronchus and Lung	U:LR,CS,FT A:LR
Malignant	Colon and Rectum	U:LR,CS,FT A:LR
Malignant	Kidney and Bladder	U:LR,CS,FT A:LR
Malignant	Prostate	U:LR,CS,FT A:LR
Malignant	Testicles	U:LR,CS,FT A:LR
Malignant	Ill-Defined Sites	U:LR A:LR
Carcinoma In Situ	Penis	U:LR,CS,FT A:LR

TABLE 7-1. (Continued)
Statistical Analysis for the Malignancy Assessment

Dependent Variables

Category	Location/ Site	Statistical Analyses
Carcinoma In Situ	Other and Unspecified Sites	U:LR A:LR
Hodgkin's Disease	--	U:LR,CS,FT A:LR
Leukemia	--	U:LR,CS,FT A:LR
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	--	U:LR,CS,FT A:LR
Skin and Systemic Neoplasms		
All	All	U:LR A:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	C	--
Race (RACE)	MIL	D	Black Non-Black
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	C	--
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	C	--

TABLE 7-1. (Continued)

Statistical Analysis for the Malignancy Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Ethnic Background (ETHBACK)	Q-SR (1985)	D	A: English, Welsh, Scottish, or Irish B: Scandinavian, German, Polish, Russian, other Slavic, Jewish, or French C: Spanish, Italian, or Greek D: Mexican, American Indian, or Asian E: African
Skin Color (SKIN)	PE (1985)	D	Dark Medium Pale Dark Peach Pale Peach
Hair Color (HAIR)	PE (1985)	D	Black Dark Brown Light Brown Blonde Red
Eye Color (EYE)	PE (1985)	D	Brown Hazel Green Gray Blue
Reaction of Skin to Sun After at Least 2 Hours, After First Exposure (SUN2HR)	Q-SR	D	Burns Painfully Burns Becomes Red No Reaction
Reaction of Skin to Sun After Repeated Exposure (SUNRPT)	Q-SR	D	Freckles With No Tan Tans Mildly Tans Moderately Tans Deep Brown

TABLE 7-1. (Continued)
Statistical Analysis for the Malignancy Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Composite Sun-Reaction Index (SUNREAC)	Q-SR	D	Burns Painfully (for SUN2HR) or Freckles With No Tan (for SUNRPT) Burns (for SUN2HR) or Tans Mildly (for SUNRPT) All Other Reactions
Average Lifetime Residential Latitude (LAT)	Q-SR (1985)	D	Latitude <37° Latitude ≥37°
Asbestos Exposure (ASB)	Q-SR	D	Yes No
Ionizing Radiation (XRAY)	Q-SR	D	Yes No
Industrial Chemical Exposure (IC)	Q-SR	D	Yes No
Herbicide Exposure (HERB)	Q-SR	D	Yes No
Insecticide Exposure (INS)	Q-SR	D	Yes No
Degreasing Chemical Exposure (DC)	Q-SR	D	Yes No
Anthracene Exposure (ANTH)	Q-SR	D	Yes No
Arsenic Exposure (ARS)	Q-SR	D	Yes No
Benzene Exposure (BENZ)	Q-SR	D	Yes No
Benzidine Exposure (BENZID)	Q-SR	D	Yes No

TABLE 7-1. (Continued)

Statistical Analysis for the Malignancy Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Chromate Exposure (CHROM)	Q-SR	D	Yes No
Coal Tar Exposure (COALTAR)	Q-SR	D	Yes No
Creosote Exposure (CREOS)	Q-SR	D	Yes No
Aminodiphenyl Exposure (AMDIPHEN)	Q-SR	D	Yes No
Chloromethyl Ether Exposure (CHLMETETH)	Q-SR	D	Yes No
Mustard Gas Exposure (MUSTGAS)	Q-SR	D	Yes No
Naphthylamine Exposure (NAPTHYL)	Q-SR	D	Yes No
Cutting Oil Exposure (CUTOIL)	Q-SR	D	Yes No
Trichloroethylene Exposure (TRICHLETH)	Q-SR	D	Yes No
Ultraviolet Light (Not Sun) Exposure (ULTLIGHT)	Q-SR	D	Yes No
Vinyl Chloride Exposure (VINCHL)	Q-SR	D	Yes No
Composite Carcinogen Exposure (CARCIN)	Q-SR	D	Yes No

TABLE 7-1. (Continued)
Statistical Analysis for the Malignancy Assessment

Dependent Variables

Data Source: All AFHS questionnaires and physical examinations

Data Form: Discrete

Cutpoints: Yes/No

Candidate Covariates for Skin Neoplasms: All covariates listed above except race.

Candidate Covariates for Systemic Neoplasms: All covariates listed above except ethnic background, skin color, hair color, eye color, reaction of skin to sun exposure variables, composite sun-reaction index, and average lifetime residential latitude.

Abbreviations

Data Source:	MIL--Air Force military records Q-SR--1987 questionnaire (self-reported) Q-SR (1985)--1985 questionnaire (self-reported); updated for participants who attended the 1987 study but not the 1985 study PE--1987 physical examination PE (1985)--1985 physical examination; updated for participants who attended the 1987 study but not the 1985 study.
Data Form:	D--Discrete analysis only
Statistical Analyses:	U--Unadjusted analyses A--Adjusted analyses
Statistical Methods:	CS--Chi-square contingency table test FT--Fisher's exact test LR--Logistic regression analysis
Other:	NOS--Not otherwise specified

TABLE 7-2.
Number of Participants With Missing Data for the
Malignancy Assessment

Variable	Variable Use	Assumption (Ranch Hands Only)		Categorized Current Dioxin	
		Minimal	Maximal	Ranch Hand	Comparison
Ethnic Background ^a	COV	13	17	16	15
Hair Color ^a	COV	0	0	0	1
Reaction of Skin to Sun After Repeated Exposure ^a	COV	0	0	0	1
Average Lifetime Residential Latitude ^a	COV	0	0	1	5
Lifetime Alcohol History	COV	6	9	9	2
Composite Carcinogen Exposure	COV	6	11	10	7

^aNon-Blacks only.
COV--Covariate (missing data).

analysis), separate analyses were performed for verified neoplasms and for the combination of verified and suspected neoplasms when suspected neoplasms were present. When a portion of an individual table presents results on the categorized current dioxin analysis, a subtitle identifies whether participants with verified or verified and suspected neoplasms were used. When no suspected neoplasms are present for a dependent variable, only tables labeled as "verified" are provided.

In some analyses, the number of participants with a neoplasm was very sparse or zero, thereby precluding an unadjusted and/or adjusted analysis. For completeness of documentation on such analyses, the relative frequencies and sample sizes are provided without the associated relative risks, confidence intervals, and p-values.

All Skin Neoplasms

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal and maximal assumptions, the unadjusted analyses of the frequency of Ranch Hands with a verified skin neoplasm (regardless of behavior or cell type) exhibited significant or marginally significant relative risks less than 1 with respect to initial dioxin (Table 7-3 [a] and [b]: Est. RR=0.77, p=0.014 and Est. RR=0.88, p=0.092, respectively). For the minimal analysis, the relative frequencies of Ranch Hands with a verified skin neoplasm were 22.9, 15.2, and 12.5 percent within the low, medium, and high initial dioxin categories. The corresponding relative frequencies of Ranch Hands under the maximal assumption were 16.6, 17.7, and 12.3 percent.

Under the minimal assumption, the adjusted analysis of the frequency of Ranch Hands with a verified skin neoplasm also exhibited a significant relative risk (Table 7-3 [c]: Adj. RR=0.77, p=0.021), but it was less than 1. Under the maximal assumption, the relative risk became nonsignificant after adjusting for age, skin reaction after at least 2 hours of sun exposure, and ethnic background (Table 7-3 [d]: p=0.278).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified skin neoplasm had a nonsignificant interaction between current dioxin and time since tour (Table 7-3 [e]: p=0.646). Although the interaction was nonsignificant, the relative risk within each time stratum was marginally significant but less than 1 (≤ 18.6 years: Est. RR=0.69, p=0.054; > 18.6 years: Est. RR=0.77, p=0.083). The relative frequencies of Ranch Hands with a verified skin neoplasm within the low, medium, and high current dioxin categories were 20.0, 16.5, and 9.3 percent for time of 18.6 years or less, and 25.9, 14.0, and 14.9 percent for time over 18.6 years.

Under the maximal assumption, the interaction of current dioxin and time was nonsignificant for the unadjusted analysis of Ranch Hands with a verified skin neoplasm (Table 7-3 [f]: p=0.253). Although the interaction was nonsignificant, the relative risk for time of 18.6 years or less was of borderline significance (Table 7-3 [f]: Est. RR=0.80, p=0.062) but less than 1. The relative frequencies of Ranch Hands with verified skin neoplasms within the later time since tour stratum (≤ 18.6 years) were 19.6, 18.4, and 9.9 percent for the low, medium, and high current dioxin categories.

TABLE 7-3.
Analysis of All Skin Neoplasms

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a) Minimal (n=489)	Low	118	22.9	0.77 (0.62,0.96)	0.014
	Medium	243	15.2		
	High	128	12.5		
b) Maximal (n=704)	Low	181	16.6	0.88 (0.75,1.02)	0.092
	Medium	344	17.7		
	High	179	12.3		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c) Minimal (n=476)	0.77 (0.61,0.97)		0.021	SUN2HR (p<0.001) ETHBACK (p=0.032)	
d) Maximal (n=687)	0.92 (0.78,1.08)		0.278	AGE (p=0.031) SUN2HR (p=0.002) ETHBACK (p=0.017)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-3. (Continued)
Analysis of All Skin Neoplasms

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=489)	≤18.6	20.0 (65)	16.5 (121)	9.3 (54)	0.69 (0.48,1.01)	0.646 ^b 0.054 ^c
	>18.6	25.9 (54)	14.0 (121)	14.9 (74)	0.77 (0.58,1.03)	0.083 ^c
f) Maximal (n=704)	≤18.6	19.6 (102)	18.4 (179)	9.9 (81)	0.80 (0.62,1.01)	0.253 ^b 0.062 ^c
	>18.6	10.3 (78)	18.7 (166)	13.3 (98)	0.96 (0.78,1.18)	0.671 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g) Minimal (n=476)	≤18.6	0.70 (0.48,1.02)	0.604 ^b 0.065 ^c	SUN2HR (p<0.001) ETHBACK (p=0.037)
	>18.6	0.80 (0.59,1.08)	0.142 ^c	
h) Maximal (n=687)	≤18.6	0.86 (0.67,1.10)	0.286 ^b 0.224 ^c	AGE (p=0.022) SUN2HR (p=0.002) ETHBACK (p=0.015)
	>18.6	1.02 (0.82,1.28)	0.835 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-3. (Continued)
Analysis of All Skin Neoplasms
(Verified)

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	13.0	All Categories		0.195
Unknown	333	17.1	Unknown vs. Background	1.38 (0.97,1.98)	0.075
Low	184	16.3	Low vs. Background	1.30 (0.84,2.04)	0.242
High	179	11.7	High vs. Background	0.89 (0.54,1.47)	0.651
Total	1,435				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	719	All Categories		0.262	AGE (p=0.138)
Unknown	324	Unknown vs. Background	1.32 (0.92,1.91)	0.134	ETHBACK (p=0.034)
Low	180	Low vs. Background	1.39 (0.89,2.19)	0.150	SUN2HR (p=0.008)
High	175	High vs. Background	0.93 (0.55,1.57)	0.778	LAT (p=0.135)
Total	1,398				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-3. (Continued)

**Analysis of All Skin Neoplasms
(Verified and Suspected)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	13.3	All Categories		0.230
Unknown	333	17.1	Unknown vs. Background	1.35 (0.95,1.93)	0.097
Low	184	16.3	Low vs. Background	1.27 (0.82,1.99)	0.285
High	179	11.7	High vs. Background	0.87 (0.53,1.44)	0.585
Total	1,435				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	719	All Categories		0.296	AGE (p=0.144) ETHBACK (p=0.086)
Unknown	324	Unknown vs. Background	1.30 (0.90,1.87)	0.162	SUN2HR (p=0.006)
Low	180	Low vs. Background	1.36 (0.87,2.14)	0.184	LAT (p=0.105)
High	175	High vs. Background	0.90 (0.53,1.52)	0.694	
Total	1,398				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

Under the minimal and the maximal assumptions, the adjusted analysis of the frequency of Ranch Hands with a skin neoplasm contained nonsignificant interactions between current dioxin and time (Table 7-3 [g] and [h]: $p=0.604$ and $p=0.286$, respectively). After adjusting for covariates under the minimal assumption (i.e., skin reaction after at least 2 hours of sun exposure and ethnic background) and under the maximal assumption (i.e., age, ethnic background, skin reaction after at least 2 hours of sun exposure), two stratum-specific relative risks, which were marginally significant in the unadjusted analysis, became nonsignificant. In both cases the unadjusted and adjusted relative risks were less than 1. Under the minimal assumption, Ranch Hands with later tours displayed a marginally significant relative risk (Adj. RR=0.70, $p=0.065$) but, again, it was less than 1.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the relative frequency of participants with a verified skin neoplasm, the overall contrast of Ranch Hands with unknown, low, and high current dioxin and Comparisons with background current dioxin was nonsignificant (Table 7-3 [i1]: $p=0.195$). Although the overall contrast was nonsignificant, the contrast of Ranch Hands in the unknown current dioxin category with Comparisons in the background category was marginally significant (Est. RR=1.38, 95% C.I.: [0.97,1.98], $p=0.075$). The adjusted analysis of participants with a verified skin neoplasm also contained a nonsignificant overall contrast (Table 7-3 [j1]: $p=0.262$). After adjusting for age, ethnic background, skin reaction after at least 2 hours of sun exposure, and average lifetime residential latitude, the unknown versus background contrast was nonsignificant ($p=0.134$), as were the other two contrasts of interest ($p \geq 0.15$ for both contrasts).

The corresponding unadjusted analysis of the combination of verified and suspected skin neoplasms contained a nonsignificant overall contrast (Table 7-3 [i2]: $p=0.230$); the unknown versus background category contrast was again marginally significant (Est. RR=1.35, 95% C.I.: [0.95,1.93], $p=0.097$). An adjusted analysis that accounted for the covariates of age, skin reaction after at least 2 hours of sun exposure, ethnic background, and average lifetime residential latitude also contained a nonsignificant overall contrast (Table 7-3 [j2]: $p=0.296$), as well as nonsignificant Ranch Hand versus Comparison contrasts ($p > 0.15$ for each contrast).

Malignant Skin Neoplasms

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the unadjusted analysis using initial dioxin, the frequencies of Ranch Hands having a verified malignant skin neoplasm (regardless of cell type) displayed a significant relative risk, less than 1, under the minimal assumption (Table 7-4 [a]: Est. RR=0.70, $p=0.014$). The relative frequencies of Ranch Hands with a verified malignant skin neoplasm were 14.4, 7.8, and 7.0 percent for the low, medium, and high initial dioxin categories. In the maximal analysis using initial dioxin, the relative risk for Ranch Hands with a verified malignant skin neoplasm was nonsignificant and also less than 1 (Table 7-4 [b]: $p=0.136$).

In the adjusted analysis of the frequency of Ranch Hands with a malignant skin neoplasm, there was a significant interaction between initial dioxin and ionizing radiation under the minimal assumption (Table 7-4 [c]: $p=0.020$). To explore this interaction, results were investigated separately for those Ranch Hands who reported exposure to ionizing

TABLE 7-4.
Analysis of Malignant Skin Neoplasms

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a) Minimal (n=489)	Low	118	14.4	0.70 (0.52,0.95)	0.014
	Medium	243	7.8		
	High	128	7.0		
b) Maximal (n=704)	Low	181	8.3	0.86 (0.70,1.05)	0.136
	Medium	344	10.8		
	High	179	6.1		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)^a	p-Value	Covariate Remarks
c) Minimal (n=476)	0.82 (0.60,1.13)**	0.212**	INIT*XRAY (p=0.020) ETHBACK (p=0.038) SUN2HR (p=0.004) SUNRPT (p=0.021) AGE*XRAY (p=0.013)
d) Maximal (n=687)	0.88 (0.71,1.11)	0.276	ETHBACK (p=0.042) SUN2HR (p=0.021) HAIR (p=0.142) AGE*LAT (p=0.039) SUNRPT*LAT (p=0.007) SUNRPT*XRAY (p=0.016)

^aRelative risk for a twofold increase in dioxin.

**Initial dioxin-by-covariate interaction (0.01 < p <= 0.05); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

INIT: Log₂ (initial dioxin).

TABLE 7-4. (Continued)
Analysis of Malignant Skin Neoplasms

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=489)	≤18.6	13.8 (65)	9.9 (121)	5.6 (54)	0.61 (0.37,0.99)	0.528 ^b 0.046 ^c
	>18.6	14.8 (54)	6.6 (121)	6.8 (74)	0.74 (0.50,1.12)	0.156 ^c
f) Maximal (n=704)	≤18.6	8.8 (102)	2.8 (179)	3.7 (81)	0.83 (0.62,1.13)	0.797 ^b 0.241 ^c
	>18.6	7.7 (78)	9.6 (166)	6.1 (98)	0.88 (0.66,1.17)	0.386 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g) Minimal (n=476)	≤18.6	0.70 (0.42,1.16)	0.335 ^b	ETHBACK (p=0.040) SUN2HR (p=0.008) SUNRPT (p=0.025) AGE*XRAY (p=0.030)
	>18.6	0.96 (0.63,1.47)	0.167 ^c	
			0.851 ^c	
h) Maximal (n=687)	≤18.6	0.88 (0.63,1.22)	0.743 ^b	ETHBACK (p=0.031) SUN2HR (p=0.018) AGE*LAT (p=0.045) SUNRPT*LAT (p=0.007) SUNRPT*XRAY (p=0.015)
	>18.6	0.95 (0.68,1.31)	0.433 ^c	
			0.740 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-4. (Continued)
Analysis of Malignant Skin Neoplasms
(Verified)

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	7.4	All Categories		0.197
Unknown	333	9.9	Unknown vs. Background	1.37 (0.87,2.15)	0.174
Low	184	9.2	Low vs. Background	1.27 (0.72,2.24)	0.417
High	179	5.0	High vs. Background	0.66 (0.32,1.36)	0.258
Total	1,435				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	718	All Categories		0.381	SUN2HR (p=0.008) SUNRPT (p=0.028)
Unknown	324	Unknown vs. Background	1.33 (0.83,2.14)	0.238	LAT (p=0.022)
Low	180	Low vs. Background	1.47 (0.81,2.65)	0.201	AGE*ETHBACK
High	175	High vs. Background	0.84 (0.40,1.78)	0.657	(p=0.025) HAIR*XRAY (p=0.039)
Total	1,397				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-4. (Continued)
Analysis of Malignant Skin Neoplasms
(Verified and Suspected)

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	7.6	All Categories		0.209
Unknown	333	9.9	Unknown vs. Background	1.34 (0.85,2.11)	0.201
Low	184	9.2	Low vs. Background	1.24 (0.70,2.19)	0.456
High	179	5.0	High vs. Background	0.65 (0.31,1.33)	0.238
Total	1,435				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	718	All Categories		0.374	SUN2HR (p=0.006) SUNRPT (p=0.022)
Unknown	324	Unknown vs. Background	1.30 (0.81,2.09)	0.276	LAT (p=0.015)
Low	180	Low vs. Background	1.44 (0.80,2.60)	0.222	AGE*ETHBACK
High	175	High vs. Background	0.83 (0.39,1.75)	0.618	(p=0.022)
Total	1,397				HAIR*XRAY (p=0.027)

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

radiation and those who reported no exposure to ionizing radiation (Appendix Table F-1). For those Ranch Hands who were not exposed to ionizing radiation, the relative risk was nonsignificant ($p=0.984$); for Ranch Hands exposed to ionizing radiation, the relative risk was significant but less than 1 (Est. RR=0.36, $p=0.029$). A model without the interaction between initial dioxin and ionizing radiation produced a nonsignificant relative risk (Table 7-4 [c]: $p=0.212$).

Under the maximal assumption, the adjusted analysis of the frequency of Ranch Hands with a malignant skin neoplasm was nonsignificant (Table 7-4 [d]: $p=0.276$).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis indicated that the relative risks for Ranch Hands with a verified malignant skin neoplasm were not significantly different between time since tour strata (Table 7-4 [e]: $p=0.528$). However, for Ranch Hands whose time since tour was 18.6 years or less, the relative risk was significant but less than 1 (Est. RR=0.61, $p=0.046$). For that time stratum, the relative frequencies of Ranch Hands with a malignant skin neoplasm within the low, medium, and high current dioxin categories were 13.8, 9.9, and 5.6 percent. Under the maximal assumption, the interaction between current dioxin and time was nonsignificant for the unadjusted analysis of verified malignant skin neoplasms (Table 7-4 [f]: $p=0.797$).

Under both the minimal and maximal assumptions, the adjusted analysis of the frequency of Ranch Hands with a malignant skin neoplasm contained a nonsignificant interaction between current dioxin and time since tour (Table 7-4 [g] and [h]: $p=0.335$ and $p=0.743$, respectively).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis for participants with a verified malignant skin neoplasm, the overall contrast of the three Ranch Hand current dioxin categories and the Comparison background current dioxin category was nonsignificant (Table 7-4 [i1]: $p=0.197$). The corresponding overall contrast for the combination of verified and suspected malignant skin neoplasms was also nonsignificant for the unadjusted analysis (Table 7-4 [i2]: $p=0.209$). The adjusted analyses for verified malignant skin neoplasms, as well as the combination of verified and suspected malignant skin neoplasms, also contained nonsignificant overall contrasts (Table 7-4 [j1] and [j2]: $p=0.381$ and $p=0.374$, respectively).

Benign Skin Neoplasms

As mentioned earlier, the statistical analyses of skin neoplasms were generally limited to non-Black participants because Blacks have a lower susceptibility to sun-induced skin cancer. An exception occurred in the statistical analysis for benign skin neoplasms. In that case, the analyses were performed separately for non-Black participants, as well as for Black and non-Black participants combined.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the unadjusted analysis using initial dioxin, the frequency of non-Black Ranch Hands with a verified benign skin neoplasm exhibited nonsignificant relative risks less than 1 under both the minimal and maximal assumptions (Table 7-5 [a1] and [b1]: $p=0.635$ and $p=0.771$).

TABLE 7-5.
Analysis of Benign Skin Neoplasms
(Non-Blacks Only)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=489)	Low	118	8.5	0.93 (0.70,1.25)	0.635
	Medium	243	7.4		
	High	128	6.3		
b1) Maximal (n=704)	Low	181	7.7	0.97 (0.79,1.20)	0.771
	Medium	344	7.0		
	High	179	6.7		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)^a	p-Value	Covariate Remarks
c1) Minimal (n=489)	0.93 (0.70,1.25)	0.635	--
d1) Maximal (n=704)	0.97 (0.79,1.20)	0.771	--

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-5. (Continued)
Analysis of Benign Skin Neoplasms
(Blacks Included)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a2) Minimal (n=521)	Low	130	8.5	0.93 (0.70,1.24)	0.609
	Medium	260	7.3		
	High	131	6.1		
b2) Maximal (n=742)	Low	185	7.6	0.97 (0.79,1.20)	0.773
	Medium	371	7.0		
	High	186	6.5		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c2) Minimal (n=521)	0.93 (0.70,1.24)		0.609	--	
d2) Maximal (n=742)	0.97 (0.79,1.20)		0.773	--	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-5. (Continued)
Analysis of Benign Skin Neoplasms
(Non-Blacks Only)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=489)	≤18.6	6.2 (65)	6.6 (121)	3.7 (54)	0.89 (0.52,1.51)	0.985 ^b 0.661 ^c
	>18.6	11.1 (54)	7.4 (121)	9.5 (74)	0.89 (0.62,1.28)	0.541 ^c
f1) Maximal (n=704)	≤18.6	9.8 (102)	5.6 (179)	6.2 (81)	0.80 (0.56,1.14)	0.165 ^b 0.220 ^c
	>18.6	2.6 (78)	9.0 (166)	8.2 (98)	1.09 (0.84,1.43)	0.516 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g1) Minimal (n=489)	≤18.6	0.89 (0.52,1.51)	0.985 ^b 0.661 ^c	--
	>18.6	0.89 (0.62,1.28)	0.541 ^c	
h1) Maximal (n=704)	≤18.6	0.80 (0.56,1.14)	0.165 ^b 0.220 ^c	--
	>18.6	1.09 (0.84,1.43)	0.516 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-5. (Continued)
Analysis of Benign Skin Neoplasms
(Blacks Included)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)^a	p-Value
		Low	Medium	High		
e2) Minimal (n=521)	≤18.6	6.9 (72)	6.3 (128)	3.7 (54)	0.85 (0.51,1.45)	0.866 ^b 0.559 ^c
	>18.6	10.3 (58)	7.6 (132)	9.1 (77)	0.90 (0.63,1.29)	0.573 ^c
f2) Maximal (n=742)	≤18.6	9.4 (106)	5.8 (191)	6.0 (83)	0.80 (0.55,1.14)	0.154 ^b 0.213 ^c
	>18.6	2.5 (79)	8.9 (179)	7.7 (104)	1.09 (0.84,1.43)	0.498 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
g2) Minimal (n=521)	≤18.6	0.85 (0.51,1.45)		0.866 ^b 0.559 ^c	--	
	>18.6	0.90 (0.63,1.29)		0.573 ^c		
h2) Maximal (n=742)	≤18.6	0.80 (0.55,1.14)		0.154 ^b 0.213 ^c	--	
	>18.6	1.09 (0.84,1.43)		0.498 ^c		

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-5. (Continued)

**Analysis of Benign Skin Neoplasms
(Non-Blacks Only)
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	6.0	All Categories		0.828
Unknown	333	7.2	Unknown vs. Background	1.23 (0.73,2.05)	0.437
Low	184	7.1	Low vs. Background	1.20 (0.63,2.28)	0.575
High	179	7.3	High vs. Background	1.24 (0.65,2.35)	0.516
Total	1,435				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	738	All Categories		0.808	HAIR (p=0.120)
Unknown	333	Unknown vs. Background	1.26 (0.75,2.11)	0.384	
Low	184	Low vs. Background	1.21 (0.64,2.31)	0.555	
High	179	High vs. Background	1.21 (0.63,2.30)	0.565	
Total	1,434				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-5. (Continued)
Analysis of Benign Skin Neoplasms
(Blacks Included)
(Verified)

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	5.9	All Categories		0.722
Unknown	345	7.5	Unknown vs. Background	1.31 (0.80,2.16)	0.285
Low	196	7.1	Low vs. Background	1.24 (0.67,2.30)	0.500
High	187	7.0	High vs. Background	1.20 (0.64,2.27)	0.572
Total	1,514				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	785	All Categories		0.680	HAIR (p=0.106)
Unknown	345	Unknown vs. Background	1.35 (0.82,2.22)	0.246	
Low	196	Low vs. Background	1.25 (0.67,2.33)	0.478	
High	187	High vs. Background	1.17 (0.62,2.22)	0.621	
Total	1,513				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

An unadjusted analysis of verified benign skin neoplasms for Black and non-Black Ranch Hands combined produced essentially the same results as the preceding analyses (Table 7-5 [a2] and [b2]: $p=0.609$ and $p=0.773$, respectively). Under each assumption, no covariates were retained in the adjusted analysis of the non-Black Ranch Hands (Table 7-5 [c1] and [d1]), as well as the combined cohort of Black and non-Black Ranch Hands (Table 7-5 [c2] and [d2]); therefore, the unadjusted and adjusted results were the same.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under both the minimal and maximal assumptions, the unadjusted analysis of verified benign skin neoplasms for non-Black Ranch Hands displayed a nonsignificant current dioxin-by-time since tour interaction (Table 7-5 [e1] and [f1]: $p=0.985$ and $p=0.165$, respectively). Combining the Black Ranch Hands with non-Black Ranch Hands also produced nonsignificant interactions (Table 7-5 [e2] and [f2]: $p=0.866$ and $p=0.154$, respectively) as well as nonsignificant relative risks within time stratum. No covariates were retained in the adjusted models for either the non-Black Ranch Hand cohort (Table 7-5 [g1] and [h1]), or after Black Ranch Hands were included in the analysis (Table 7-5 [g2] and [h2]); hence the unadjusted and adjusted results were identical.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted analysis indicated that non-Black Ranch Hands in the unknown, low, and high current dioxin categories and non-Black Comparisons in the background current dioxin category were not significantly different with respect to the relative frequency of participants with a verified benign skin neoplasm (Table 7-5 [i1]: $p=0.828$). Although nonsignificant, each of the Ranch Hand versus Comparison contrasts had a relative risk over 1. Including Blacks with non-Blacks also resulted in nonsignificant overall and individual contrasts with associated relative risks greater than 1 (Table 7-5 [i2]: $p=0.722$).

The adjusted analysis also produced a nonsignificant overall contrast for the non-Black participants (Table 7-5 [j1]: $p=0.808$). An adjusted analysis performed with Black and non-Black participants combined also exhibited a nonsignificant overall contrast (Table 7-5 [j2]: $p=0.680$). Although nonsignificant, the relative risks for the individual contrasts were greater than 1.

Because there were no Comparisons with a suspected benign skin neoplasm, analysis of combined verified and suspected neoplasms was not performed.

Skin Neoplasms of Uncertain Behavior or Unspecified Nature

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal assumption, no Ranch Hands had a verified skin neoplasm of uncertain behavior or unspecified nature. Under the maximal assumption, only one Ranch Hand in the low initial dioxin category had this type of verified neoplasm (Table 7-6 [a] and [b]). Due to such sparse data, unadjusted and adjusted analyses were not performed.

TABLE 7-6.

**Analysis of Skin Neoplasms of Uncertain
Behavior or Unspecified Nature**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b) Maximal (n=704)	Low	181	0.6	--	--
	Medium	344	0.0		
	High	179	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c) Minimal (n=489)	--		--	--	
d) Maximal (n=704)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-6. (Continued)

Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e) Minimal (n=489)	≤18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f) Maximal (n=704)	≤18.6	1.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.0 (166)	0.0 (98)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g) Minimal (n=489)	≤18.6	--	--	--
	>18.6	--	--	--
h) Maximal (n=704)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-6. (Continued)

**Analysis of Skin Neoplasms of Uncertain
Behavior or Unspecified Nature
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.3	Unknown vs. Background	--	0.622
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-6. (Continued)

**Analysis of Skin Neoplasms of Uncertain
Behavior or Unspecified Nature
(Verified and Suspected)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.1	All Categories		--
Unknown	333	0.3	Unknown vs. Background	2.22 (0.14,35.65)	0.999
Low	184	0.0	Low vs. Background	--	0.999
High	179	0.0	High vs. Background	--	0.999
Total	1,435				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Due to sparse data, unadjusted and adjusted analyses were not performed (Table 7-6 [e] and [f]).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

With respect to the categorized current dioxin analysis, the one Ranch Hand with a verified skin neoplasm of uncertain behavior or unspecified nature was in the unknown current dioxin category (Table 7-6 [i1]). Because of the sparse number of neoplasms, only the contrast of the unknown category versus the background category was performed; it was found to be nonsignificant ($p=0.622$). For the combination of verified and suspected skin neoplasms, one Comparison had a suspected skin neoplasm of uncertain behavior or unspecified nature (Table 7-6 [i2]). The contrasts of interest were nonsignificant ($p=0.999$ for each contrast). Adjusted analyses were not performed due to the sparse number of neoplasms.

Basal Cell Carcinoma—All Sites and by Location/Site

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified basal cell carcinoma at any site contained a significant relative risk less than 1 with respect to initial dioxin (Table 7-7 [a1]: Est. RR=0.73, $p=0.037$). The relative frequencies were 11.0, 7.4, and 5.5 percent for the low, medium, and high initial dioxin categories. The corresponding analysis under the maximal assumption was nonsignificant (Table 7-7 [b1]: $p=0.114$). Under the minimal assumption, the adjusted analysis of verified basal cell carcinoma produced a nonsignificant relative risk less than 1 (Table 7-7 [c1]: $p=0.317$) after adjusting for the two skin reaction to sun exposure covariates, ethnic background, and an interaction between age and ionizing radiation. Under the maximal assumption, the adjusted analysis also was nonsignificant for an association with initial dioxin (Table 7-7 [d1]: $p=0.449$).

Under both assumptions of the unadjusted analysis, the relative risk of the frequency of Ranch Hands with a verified basal cell carcinoma on the ear, face, head, and neck was significant but less than 1 (Table 7-7 [a2] and [b2]: Est. RR=0.51, $p=0.002$ and Est. RR=0.71, $p=0.017$, respectively). In the minimal analysis, the relative frequencies were 8.5, 4.9, and 1.6 percent for the low, medium, and high initial dioxin categories. The corresponding relative frequencies for the maximal analysis were 5.5, 6.4, and 1.7 percent. The covariates of age, skin reaction after at least 2 hours of sun exposure, and ethnic background were retained in the adjusted model. Under the minimal assumption, the relative risk remained significant but less than 1 (Table 7-7 [c2]: Adj. RR=0.59, $p=0.025$). Under the maximal assumption, the relative risk became marginally significant and also remained less than 1 (Table 7-7 [d2]: Adj. RR=0.77, $p=0.087$).

Under the minimal and maximal assumptions, the unadjusted analyses using initial dioxin contained nonsignificant relative risks that were equal to or less than 1 for verified basal cell carcinoma on the trunk (Table 7-7 [a3] and [b3]: $p=0.632$ and $p=0.999$, respectively). The adjusted analyses produced relative risks slightly greater than 1 but they were nonsignificant (Table 7-7 [c3] and [d3]: $p=0.954$ and $p=0.684$).

TABLE 7-7.

**Analysis of Basal Cell Carcinoma
(All Sites Combined)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=489)	Low	118	11.0	0.73 (0.53,1.00)	0.037
	Medium	243	7.4		
	High	128	5.5		
b1) Maximal (n=704)	Low	181	8.3	0.84 (0.68,1.05)	0.114
	Medium	344	9.0		
	High	179	5.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c1) Minimal (n=476)	0.85 (0.60,1.18)		0.317	ETHBACK (p=0.073) SUN2HR (p=0.063) SUNRPT (p=0.029) AGE*XRAY (p=0.024)	
d) Maximal (n=687)	0.92 (0.72,1.16)		0.449	ETHBACK (p=0.046) SUN2HR (p=0.068) SUNRPT (p=0.017) AGE*XRAY (p=0.045)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Ear, Face, Head, and Neck)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a2) Minimal (n=489)	Low	118	8.5	0.51 (0.31,0.83)	0.002
	Medium	243	4.9		
	High	128	1.6		
b2) Maximal (n=704)	Low	181	5.5	0.71 (0.53,0.96)	0.017
	Medium	344	6.4		
	High	179	1.7		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)^a	p-Value	Covariate Remarks
c2) Minimal (n=476)	0.59 (0.36,0.98)	0.025	AGE (p=0.077) SUN2HR (p=0.003) ETHBACK (p=0.125)
d2) Maximal (n=687)	0.77 (0.56,1.05)	0.087	AGE (p=0.011) SUN2HR (p=0.001) ETHBACK (p=0.092)

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Trunk)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a3) Minimal (n=489)	Low	118	3.4	0.89 (0.54,1.46)	0.632
	Medium	243	1.6		
	High	128	3.1		
b3) Maximal (n=704)	Low	181	1.7	1.00 (0.70,1.43)	0.999
	Medium	344	2.6		
	High	179	2.2		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)^a	p-Value	Covariate Remarks
c3) Minimal (n=489)	1.01 (0.62,1.67)	0.954	AGE (p=0.033)
d3) Maximal (n=704)	1.08 (0.75,1.57)	0.684	AGE (p=0.012) SUNRPT (p<0.001)

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Upper Extremities)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.) ^a	p-Value
a4) Minimal (n=489)	Low	118	0.8	0.45 (0.08,2.68)	0.305
	Medium	243	0.4		
	High	128	0.0		
b4) Maximal (n=704)	Low	181	1.1	0.62 (0.24,1.58)	0.264
	Medium	344	0.6		
	High	179	0.0		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c4) Minimal (n=489)	--	--	--
d4) Maximal (n=704)	0.62 (0.24,1.58)	0.264	--

^aRelative risk for a twofold increase in dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Lower Extremities)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a5) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b5) Maximal (n=704)	Low	181	0.0	--	--
	Medium	344	0.0		
	High	179	0.0		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c5) Minimal (n=489)	--	--	--
d5) Maximal (n=704)	--	--	--

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Other Sites and NOS)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a6) Minimal (n=489)	Low	118	0.0	1.32 (0.64,2.69)	0.469
	Medium	243	1.2		
	High	128	0.8		
b6) Maximal (n=704)	Low	181	0.0	1.58 (0.87,2.86)	0.151
	Medium	344	0.6		
	High	179	1.1		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)^a	p-Value	Covariate Remarks
c6) Minimal (n=489)	1.34 (0.64,2.81)	0.458	SUN2HR (p=0.101)
d6) Maximal (n=704)	1.62 (0.87,3.01)	0.143	SUN2HR (p=0.099)

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(All Sites Combined)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=489)	<18.6	9.2 (65)	9.1 (121)	5.6 (54)	0.71 (0.43,1.16)	0.942 ^b 0.167 ^c
	>18.6	13.0 (54)	5.8 (121)	5.4 (74)	0.69 (0.43,1.09)	0.110 ^c
f1) Maximal (n=704)	<18.6	8.8 (102)	10.6 (179)	3.7 (81)	0.84 (0.61,1.16)	0.999 ^b 0.291 ^c
	>18.6	6.4 (78)	9.0 (166)	4.1 (98)	0.84 (0.62,1.16)	0.289 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g1) Minimal (n=476)	<18.6	0.77 (0.46,1.28)	0.759 ^b 0.312 ^c	ETHBACK (p=0.068) SUN2HR (p=0.128) SUNRPT (p=0.019) AGE*XRAY (p=0.020)
	>18.6	0.86 (0.53,1.39)	0.526 ^c	
h1) Maximal (n=687)	<18.6	0.87 (0.68,1.12)	0.725 ^b 0.280 ^c	ETHBACK (p=0.035) SUN2HR (p=0.118) AGE*XRAY (p=0.047) SUNRPT*XRAY(p=0.029)
	>18.6	0.95 (0.74,1.21)	0.623 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Ear, Face, Head, and Neck)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e2) Minimal (n=489)	<18.6	6.2 (65)	5.8 (121)	1.9 (54)	0.58 (0.29,1.17)	0.282 ^b 0.127 ^c
	>18.6	13.0 (54)	3.3 (121)	1.4 (74)	0.31 (0.13,0.76)	0.011 ^c
f2) Maximal (n=704)	<18.6	5.9 (102)	7.3 (179)	1.2 (81)	0.74 (0.49,1.13)	0.755 ^b 0.159 ^c
	>18.6	2.6 (78)	7.2 (166)	1.0 (98)	0.67 (0.42,1.06)	0.087 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g2) Minimal (n=476)	<18.6	0.69 (0.34,1.39)	0.349 ^b 0.296 ^c	AGE (p=0.123) SUN2HR (p=0.003)
	>18.6	0.41 (0.17,0.99)	0.047 ^c	ETHBACK (p=0.133)
h2) Maximal (n=687)	<18.6	0.82 (0.52,1.28)	0.776 ^b 0.375 ^c	AGE (p=0.009) SUN2HR (p=0.001)
	>18.6	0.74 (0.45,1.23)	0.246 ^c	ETHBACK (p=0.084)

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Trunk)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e3) Minimal (n=489)	<18.6	3.1 (65)	2.5 (121)	3.7 (54)	0.88 (0.42,1.84)	0.997 ^b 0.730 ^c
	>18.6	3.7 (54)	0.8 (121)	2.7 (74)		0.88 (0.42,1.84)
f3) Maximal (n=704)	<18.6	2.9 (102)	2.8 (179)	2.5 (81)	0.99 (0.60,1.64)	0.906 ^b 0.964 ^c
	>18.6	1.3 (78)	1.8 (166)	2.0 (98)		1.03 (0.60,1.79)

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g3) Minimal (n=489)	<18.6	1.19 (0.57,2.50)	0.804 ^b 0.646 ^c	AGE (p=0.020) SUNRPT (p=0.001)
	>18.6	1.05 (0.51,2.17)	0.901 ^c	
h3) Maximal (n=704)	<18.6	1.19 (0.69,2.06)	0.887 ^b 0.526 ^c	AGE (p=0.007) SUNRPT (p<0.001)
	>18.6	1.13 (0.63,2.01)	0.687 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Upper Extremities)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e4) Minimal (n=489)	<18.6	0.0 (65)	0.8 (121)	0.0 (54)	--	--
	>18.6	1.9 (54)	0.0 (121)	0.0 (74)	--	--
f4) Maximal (n=704)	<18.6	0.0 (102)	0.6 (179)	0.0 (81)	--	--
	>18.6	2.6 (78)	0.6 (166)	0.0 (98)	0.25 (0.04,1.59)	0.141 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g4) Minimal (n=489)	<18.6	--	--	--
	>18.6	--	--	--
h4) Maximal (n=704)	<18.6	--	--	SUNRPT (p=0.111)
	>18.6	0.15 (0.01,1.81)	0.136 ^c	

^aRelative risk for a twofold increase in dioxin.

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Lower Extremities)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e5) Minimal (n=489)	<18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f5) Maximal (n=704)	<18.6	0.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.0 (166)	0.0 (98)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g5) Minimal (n=489)	<18.6	--	--	--
	>18.6	--	--	--
h5) Maximal (n=704)	<18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Other Sites and NOS)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e6) Minimal (n=489)	<18.6	0.0 (65)	0.8 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	1.7 (121)	1.4 (74)	1.29 (0.59,2.86)	0.523 ^c
f6) Maximal (n=704)	<18.6	0.0 (102)	0.6 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	1.2 (166)	1.0 (98)	1.52 (0.77,2.98)	0.224 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g6) Minimal (n=489)	<18.6	--	--	SUN2HR (p=0.092)
	>18.6	1.32 (0.58,2.99)	0.509 ^c	
h6) Maximal (n=704)	<18.6	--	--	SUN2HR (p=0.093)
	>18.6	1.57 (0.78,3.16)	0.209 ^c	

^aRelative risk for a twofold increase in dioxin.

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-7. (Continued)

**Analysis of Basal Cell Carcinoma
(All Sites Combined)
(Verified)**

ii) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	6.6	All Categories		0.117
Unknown	333	9.0	Unknown vs. Background	1.39 (0.87,2.24)	0.171
Low	184	8.7	Low vs. Background	1.34 (0.74,2.42)	0.329
High	179	3.9	High vs. Background	0.57 (0.26,1.29)	0.177
Total	1,435				

ji) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	718	All Categories		0.205	SUN2HR (p=0.011) SUNRPT (p=0.052)
Unknown	324	Unknown vs. Background	1.37 (0.84,2.26)	0.208	LAT (p=0.025)
Low	180	Low vs. Background	1.54 (0.84,2.82)	0.124	AGE*ETHBACK
High	175	High vs. Background	0.71 (0.31,1.63)	0.478	(p=0.025) HAIR*XRAY (p=0.039)
Total	1,397				

Note: Background (Comparisons): Current Dioxin <10 ppt.
 Unknown (Ranch Hands): Current Dioxin <10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin <33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-7. (Continued)

**Analysis of Basal Cell Carcinoma
(Ear, Face, Head, and Neck)
(Verified)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	5.1	All Categories		0.019
Unknown	333	6.6	Unknown vs. Background	1.30 (0.76,2.24)	0.336
Low	184	5.4	Low vs. Background	1.06 (0.52,2.17)	0.873
High	179	1.1	High vs. Background	0.21 (0.05,0.87)	0.032
Total	1,435				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	718	All Categories		0.087	AGE (p=0.037) ETHBACK (p=0.021)
Unknown	324	Unknown vs. Background	1.19 (0.68,2.10)	0.541	HAIR (p=0.092)
Low	180	Low vs. Background	1.18 (0.57,2.45)	0.662	SUN2HR (p=0.038)
High	175	High vs. Background	0.26 (0.06,1.08)	0.063	SUNRPT (p=0.041) LAT (p=0.038)
Total	1,397				

Note: Background (Comparisons): Current Dioxin <10 ppt.
 Unknown (Ranch Hands): Current Dioxin <10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin <33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Trunk)
(Verified)

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	1.4	All Categories		0.765
Unknown	333	2.1	Unknown vs. Background	1.57 (0.59,4.15)	0.368
Low	184	1.6	Low vs. Background	1.21 (0.33,4.44)	0.776
High	179	2.2	High vs. Background	1.67 (0.52,5.38)	0.393
Total	1,435				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	738	All Categories		0.641	AGE (p=0.041) SUNRPT (p=0.003)
Unknown	333	Unknown vs. Background	1.59 (0.60,4.25)	0.351	
Low	184	Low vs. Background	1.28 (0.35,4.75)	0.709	
High	179	High vs. Background	2.06 (0.62,6.83)	0.238	
Total	1,434				

Note: Background (Comparisons): Current Dioxin <10 ppt.
 Unknown (Ranch Hands): Current Dioxin <10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin <33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Upper Extremities)
(Verified)

i4) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.5	All Categories		0.633
Unknown	333	0.9	Unknown vs. Background	1.67 (0.37,7.51)	0.754
Low	184	0.5	Low vs. Background	1.00 (0.11,9.04)	0.999
High	179	0.0	High vs. Background	--	0.838
Total	1,435				

j4) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	734	All Categories		0.567	AGE (p=0.083) LAT (p=0.124)
Unknown	332	Unknown vs. Background	1.78 (0.39,8.07)	0.455	
Low	184	Low vs. Background	1.10 (0.12,9.98)	0.934	
High	179	High vs. Background	--	--	
Total	1,429				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.
 Note: Background (Comparisons): Current Dioxin <10 ppt.
 Unknown (Ranch Hands): Current Dioxin <10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin <33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-7. (Continued)

**Analysis of Basal Cell Carcinoma
(Lower Extremities)
(Verified)**

i5) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.0	Unknown vs. Background	--	--
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j5) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin <10 ppt.
 Unknown (Ranch Hands): Current Dioxin <10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin <33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-7. (Continued)
Analysis of Basal Cell Carcinoma
(Other Sites and NOS)
(Verified)

i6) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.1	All Categories		0.011
Unknown	333	0.0	Unknown vs. Background	--	0.999
Low	184	1.6	Low vs. Background	12.23 (1.27,118.3)	0.053
High	179	0.6	High vs. Background	4.15 (0.26,66.61)	0.704
Total	1,435				

j6) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		0.035	SUN2HR (p=0.070)
Low	184	Low vs. Background	13.34 (1.40,127.1)	0.024	
High	179	High vs. Background	3.93 (0.25,62.34)	0.332	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin <10 ppt.
 Unknown (Ranch Hands): Current Dioxin <10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin <33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

Under the minimal assumption, there were two Ranch Hands with a verified basal cell carcinoma on the upper extremities. Under the maximal assumption, there were four Ranch Hands with a verified basal cell carcinoma on the upper extremities. Both unadjusted analyses were nonsignificant with relative risks less than 1 for an association with initial dioxin (Table 7-7 [a4] and [b4]: $p=0.305$ and $p=0.264$, respectively). Because of the sparse number of neoplasms under the minimal assumption, adjusted analyses were not performed. Under the maximal assumption, no covariates were retained in the adjusted model; therefore, the results of the unadjusted and the adjusted analyses were identical.

Under the minimal and maximal assumptions, there were no Ranch Hands with a verified basal cell carcinoma on the lower extremities (Table 7-7 [a5] and [b5]).

Under the minimal and maximal assumptions, four Ranch Hands had a verified basal cell carcinoma for other sites and sites NOS. The unadjusted analysis produced relative risks greater than 1 but the risks were not significant (Table 7-7 [a6] and [b6]: $p=0.469$ and $p=0.151$, respectively). Adjusted analyses also produced nonsignificant relative risks (Table 7-7 [c6] and [d6]: $p=0.458$ and $p=0.143$, respectively).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under both assumptions, the unadjusted analysis of the frequency of Ranch Hands with a verified basal cell carcinoma for all sites combined exhibited a nonsignificant interaction between current dioxin and time since tour (Table 7-7 [e1] and [f1]: $p=0.942$ and $p=0.999$). Under the minimal and the maximal assumptions, the adjusted analyses also had nonsignificant current dioxin-by-time interactions (Table 7-7 [g1] and [h1]: $p=0.759$ and $p=0.725$). For each of these analyses, the relative risk within each individual time stratum was nonsignificant and less than 1.

Under both assumptions, the unadjusted analysis of Ranch Hands with a verified basal cell carcinoma on the ear, face, head, and neck displayed a nonsignificant current dioxin-by-time interaction (Table 7-7 [e2] and [f2]: $p=0.282$ and $p=0.755$); thus, the relative risks within each time stratum did not differ significantly. However, in the minimal analysis, there was a significant relative risk less than 1 for Ranch Hands with tours over 18.6 years (Table 7-7 [e2]: Est. RR=0.31, $p=0.011$). In the maximal analysis, there was a marginally significant relative risk (Table 7-7 [f2]: Est. RR=0.67, $p=0.087$) also less than 1 for the same time stratum. In the former analysis, the relative frequencies of Ranch Hands with a verified basal cell carcinoma on the ear, face, head, and neck were 13.0, 3.3, and 1.4 percent within the low, medium, and high current dioxin categories for Ranch Hands with earlier tours. In the maximal analysis, the corresponding relative frequencies were 2.6, 7.2, and 1.0 percent.

Under the minimal assumption, the adjusted analysis of the frequency of Ranch Hands with a basal cell carcinoma on the ear, face, head, and neck contained a nonsignificant interaction between current dioxin and time (Table 7-7 [g2]: $p=0.349$). For Ranch Hands with time over 18.6 years, however, the relative risk was significant but less than 1 (Adj. RR=0.41, $p=0.047$). Under the maximal assumption, the interaction of current dioxin and time was nonsignificant (Table 7-7 [h2]: $p=0.776$) as were the relative risks for the individual time stratum after adjusting for age, skin reaction after at least 2 hours of sun exposure, and ethnic background.

In the unadjusted analysis of Ranch Hands with a verified basal cell carcinoma on the trunk, the interaction of current dioxin and time since tour was nonsignificant for both assumptions (Table 7-7 [e3] and [f3]: $p=0.997$ and $p=0.906$). The adjusted analysis also contained nonsignificant interactions between current dioxin and time (Table 7-7 [g3] and [h3]: $p=0.804$ and $p=0.887$). In the adjusted analysis, the relative risks associated for each time stratum were greater than 1 but nonsignificant.

In the unadjusted analysis of verified basal cell carcinoma on the upper extremities under the minimal assumption, each time since tour stratum contained only one Ranch Hand with the neoplasm of interest. Because of the sparse number of Ranch Hands with a basal cell carcinoma on the upper extremities, the relative risks, confidence intervals, and p-values were not reported for both the unadjusted and the adjusted analyses under the minimal assumption. Under the maximal assumption, one Ranch Hand with time of 18.6 years or less had a verified basal cell carcinoma on the upper extremities; three Ranch Hands had this particular skin neoplasm for time over 18.6 years. Due to the sparse number of basal cell carcinomas on the upper extremities for Ranch Hands with later tours, the relative risk, confidence interval, and p-value were not reported for that time stratum, as well as the p-value associated with the interaction of current dioxin and time. For the other time stratum, the relative risk was nonsignificant and less than 1 (Table 7-7 [f4]: $p=0.141$). Under the maximal assumption, an adjusted model also yielded a nonsignificant relative risk for time over 18.6 years (Table 7-7 [h4]: $p=0.136$).

No Ranch Hands had a verified basal cell carcinoma on the lower extremities (Table 7-7 [e5] and [f5]).

In the unadjusted analysis under each assumption, one Ranch Hand had a verified basal cell carcinoma for other sites and sites NOS with time of 18.6 years or less and three Ranch Hands had a verified basal cell carcinoma for other sites and sites NOS with time over 18.6 years. Due to the sparse number of Ranch Hands with later tours, the relative risk, confidence interval, and p-value were not reported for that time stratum, as well as the p-value associated with the interaction of current dioxin and time. For the earlier time stratum (over 18.6 years), the relative risk for verified basal cell carcinoma was nonsignificant in each unadjusted analysis (Table 7-7 [e6] and [f6]: $p=0.523$ and $p=0.224$). Corresponding adjusted analyses for time over 18.6 years also contained nonsignificant relative risks (Table 7-7 [g6] and [h6]: $p=0.509$ and $p=0.209$).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of verified basal cell carcinoma for all sites combined, the relative frequencies of participants with disease were not significantly different among Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background current dioxin category (Table 7-7 [i1]: $p=0.117$). The overall contrast for the corresponding adjusted analysis was also nonsignificant (Table 7-7 [j1]: $p=0.205$). There were no participants with suspected basal cell carcinoma.

In the unadjusted analysis for verified basal cell carcinoma on the ear, face, head, and neck, the relative frequencies differed significantly among Ranch Hands with unknown, low, and high current dioxin and Comparisons with background current dioxin (Table 7-7 [i2]:

p=0.019). The relative frequencies for background, unknown, low, and high current dioxin were 5.1, 6.6, 5.4, and 1.1 percent. The high versus background contrast was significant (p=0.032) but the relative risk was less than 1 (Est. RR=0.21, 95% C.I.: [0.05,0.87]). The unknown versus background and low versus background contrasts had relative risks greater than 1 but they were nonsignificant (p=0.336 and p=0.873, respectively). An adjusted model that retained six covariates (age, ethnic background, the two skin reaction to sun exposure variables, hair color, and average lifetime residential latitude) exhibited a marginally significant overall contrast (Table 7-7 [j2]: p=0.087). The high versus background contrast was also marginally significant (p=0.063) but the relative risk was less than 1 (Adj. RR=0.26, 95% C.I.: [0.06,1.08]). The unknown versus background and low versus background contrasts had relative risks greater than 1 but were nonsignificant (p=0.541 and p=0.662, respectively).

The unadjusted and the adjusted analyses for verified basal cell carcinoma on the trunk contained nonsignificant overall contrasts for the three current dioxin categories of the Ranch Hands and the background current dioxin category of the Comparisons (Table 7-7 [i3] and [j3]: p=0.765 and p=0.641, respectively). The individual contrasts had associated relative risks greater than 1 but were nonsignificant.

Four Ranch Hands and four Comparisons had a verified basal cell carcinoma on the upper extremities. Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category exhibited nonsignificant overall unadjusted and adjusted contrasts for verified basal cell carcinomas on the upper extremities (Table 7-7 [i4] and [j4]: p=0.633 and p=0.567, respectively).

No participants had a verified basal cell carcinoma on the lower extremities (Table 7-7 [i5]).

Four Ranch Hands (three in the low category, one in the high category) and one Comparison had a verified basal cell carcinoma for other sites and sites NOS. In the unadjusted analysis, the overall contrast of the relative frequencies of Ranch Hands with unknown, low, and high current dioxin and Comparisons with background current dioxin was significant (Table 7-7 [i6]: p=0.011). The relative frequencies for the background, unknown, low, and high current dioxin categories were 0.1, 0.0, 1.6, and 0.6 percent. The contrast of Ranch Hands in the unknown current dioxin category with Comparisons in the background category was nonsignificant (p=0.999). The contrast using Ranch Hands in the low current dioxin category was marginally significant (Est. RR=12.23, 95% C.I.: [1.27,118.23], p=0.053). The high versus background contrast also had a relative risk over 1 but it was nonsignificant (p=0.704) and lower than the relative risk of the low versus background contrast. After adjusting for skin reaction after at least 2 hours of sun exposure, the overall contrast remained significant (Table 7-7 [j6]: p=0.035). The low versus background contrast became significant (Adj. RR=13.34, 95% C.I.: [1.40,127.1], p=0.024) and the high versus background contrast remained nonsignificant (p=0.332).

Sun Exposure-Related Malignant Skin Neoplasms—All Sites and by Location/Site

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified sun exposure-related malignant skin neoplasm for all sites combined contained a significant relative risk with respect to initial dioxin (Table 7-8 [a1]: Est. RR=0.70, p=0.014) but it was less than 1. The relative frequencies were 13.6, 7.8, and 6.3 percent for the low, medium, and high initial dioxin categories. The corresponding unadjusted analysis under the maximal assumption was nonsignificant with a relative risk less than 1 (Table 7-8 [b1]: p=0.103).

Under the minimal assumption, the adjusted analysis contained a significant interaction between initial dioxin and ionizing radiation (Table 7-8 [c1]: p=0.020). To investigate the interaction, the association with initial dioxin was examined separately for Ranch Hands who reported being exposed and not being exposed to ionizing radiation (Appendix Table F-1). For those Ranch Hands who had not reported exposure to ionizing radiation, the relative risk was nonsignificant (p=0.960); for Ranch Hands who reported exposure to ionizing radiation, the relative risk was significant but less than 1 (Adj. RR=0.36, p=0.029). A model without the interaction between initial dioxin and ionizing radiation displayed a nonsignificant relative risk (p=0.212). Under the maximal assumption, the adjusted analysis of the frequency of Ranch Hands with a sun exposure-related malignant skin neoplasm was nonsignificant (Table 7-8 [d1]: p=0.235).

The unadjusted analyses for a verified sun exposure-related malignant skin neoplasm on the ear, face, head, and neck displayed significant relative risks less than 1 under each assumption (Table 7-8 [a2] and [b2]: Est. RR=0.56, p=0.003 and Est. RR=0.75, p=0.031). Under the minimal assumption, the relative frequencies of Ranch Hands with a verified sun exposure-related malignant skin neoplasm on the ear, face, head, and neck were 9.3, 5.3, and 2.3 percent for the low, medium, and high initial dioxin categories. In the maximal analysis, the corresponding relative frequencies for low, medium, and high initial dioxin were 5.5, 7.3, and 2.2 percent. Under the minimal assumption, the adjusted analysis contained a significant relative risk but it remained less than 1 (Table 7-8 [c2]: Adj. RR=0.65, p=0.047). Under the maximal assumption, adjustment for age, ethnic background, hair color, skin reaction after at least 2 hours of sun exposure, and average lifetime residential latitude produced a nonsignificant relative risk that also was less than 1 (Table 7-8 [d2]: p=0.197).

In the unadjusted analysis of the frequency of Ranch Hands with a verified sun exposure-related malignant skin neoplasm on the trunk, the estimated relative risks were nonsignificant and less than 1 under both assumptions (Table 7-8 [a3] and [b3]: p=0.132 and p=0.648). In addition, both adjusted analyses produced nonsignificant relative risks (Table 7-8 [c3] and [d3]: p=0.389 and p=0.967).

For verified sun exposure-related malignant skin neoplasms on the upper extremities, the minimal analysis contained three Ranch Hands and the maximal analysis contained five Ranch Hands with these skin neoplasms. Under both assumptions, the relative risks were nonsignificant for the unadjusted analyses using initial dioxin (Table 7-8 [a4] and [b4]: p=0.908 and p=0.890). Due to the small number of Ranch Hands with a verified sun exposure-related malignant skin neoplasm on the upper extremities, adjusted analyses were

TABLE 7-8.

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(All Sites Combined)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=489)	Low	118	13.6	0.70 (0.51,0.95)	0.014
	Medium	243	7.8		
	High	128	6.3		
b1) Maximal (n=704)	Low	181	8.3	0.85 (0.69,1.04)	0.103
	Medium	344	10.5		
	High	179	5.6		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c1) Minimal (n=476)	0.82 (0.59,1.13)**		0.212**	INIT*XRAY (p=0.020) ETHBACK (p=0.047) SUN2HR (p=0.005) SUNRPT (p=0.008) AGE*XRAY (p=0.015)	
d1) Maximal (n=687)	0.87 (0.69,1.10)		0.235	AGE (p=0.002) ETHBACK (p=0.032) SUN2HR (p=0.017) SUNRPT*LAT (p=0.008) SUNRPT*XRAY (p=0.029)	

^aRelative risk for a twofold increase in dioxin.

**Log₂ (initial dioxin)-by-covariate interaction (0.01<p≤0.05); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Ear, Face, Head, and Neck)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a2) Minimal (n=489)	Low	118	9.3	0.56 (0.36,0.86)	0.003
	Medium	243	5.3		
	High	128	2.3		
b2) Maximal (n=704)	Low	181	5.5	0.75 (0.58,0.99)	0.031
	Medium	344	7.3		
	High	179	2.2		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c2) Minimal (n=476)	0.65 (0.41,1.03)		0.047	AGE (p=0.042) SUN2HR (p<0.001) ETHBACK (p=0.097)	
d2) Maximal (n=687)	0.83 (0.61,1.11)		0.197	AGE (p=0.021) ETHBACK (p=0.083) HAIR (p=0.099) SUN2HR (p<0.001) LAT (p=0.072)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-8. (Continued)
Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Trunk)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.) ^a	p-Value
a3) Minimal (n=489)	Low	118	5.9	0.69 (0.41,1.16)	0.132
	Medium	243	1.6		
	High	128	3.1		
b3) Maximal (n=704)	Low	181	1.7	0.92 (0.66,1.30)	0.648
	Medium	344	3.5		
	High	179	2.2		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption			Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c3) Minimal (n=489)			0.81 (0.48,1.34)	0.389	AGE (p=0.016) SUNRPT (p<0.001)
d3) Maximal (n=704)			0.99 (0.69,1.43)	0.967	AGE (p=0.004) SUNRPT (p<0.001)

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Upper Extremities)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a4) Minimal (n=489)	Low	118	0.8	1.06 (0.43,2.62)	0.908
	Medium	243	0.4		
	High	128	0.8		
b4) Maximal (n=704)	Low	181	1.1	0.96 (0.50,1.83)	0.890
	Medium	344	0.6		
	High	179	0.6		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c4) Minimal (n=489)	--		--	--	
d4) Maximal (n=704)	0.95 (0.49,1.86)		0.889	SUN2HR (p=0.131)	

^aRelative risk for a twofold increase in dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Lower Extremities)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a5) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b5) Maximal (n=704)	Low	181	0.0	--	--
	Medium	344	0.0		
	High	179	0.0		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)^a	p-Value	Covariate Remarks
c5) Minimal (n=489)	--	--	--
d5) Maximal (n=704)	--	--	--

^aRelative risk for a twofold increase in dioxin.

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Other Sites and NOS)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a6) Minimal (n=489)	Low	118	0.0	1.32 (0.64,2.69)	0.469
	Medium	243	1.2		
	High	128	0.8		
b6) Maximal (n=704)	Low	181	0.0	1.58 (0.87,2.86)	0.151
	Medium	344	0.6		
	High	179	1.1		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c6) Minimal (n=489)	1.34 (0.64,2.81)		0.458	SUN2HR (p=0.101)	
d6) Maximal (n=704)	1.62 (0.87,3.01)		0.143	SUN2HR (p=0.099)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(All Sites Combined)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=489)	≤18.6	12.3 (65)	9.9 (121)	5.6 (54)	0.63 (0.38,1.03)	0.694 ^b 0.065 ^c
	>18.6	14.8 (54)	5.8 (121)	6.8 (74)	0.72 (0.47,1.10)	0.125 ^c
f1) Maximal (n=704)	≤18.6	8.8 (102)	12.3 (179)	3.7 (81)	0.84 (0.62,1.14)	0.910 ^b 0.253 ^c
	>18.6	7.7 (78)	9.6 (166)	5.1 (98)	0.86 (0.64,1.15)	0.305 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a		p-Value	Covariate Remarks	
g1) Minimal (n=476)	≤18.6	0.72 (0.43,1.20)		0.452 ^b 0.207 ^c	ETHBACK (p=0.052) SUN2HR (p=0.010) SUNRPT (p=0.010) AGE*XRAY (p=0.034)	
	>18.6	0.93 (0.59,1.45)		0.739 ^c		
h1) Maximal (n=687)	≤18.6	0.96 (0.69,1.33)		0.992 ^b 0.784 ^c	AGE (p<0.001) ETHBACK (p=0.027) SUN2HR (p=0.027) SUNRPT (p=0.004)	
	>18.6	0.96 (0.69,1.32)		0.782 ^c		

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-8. (Continued)
Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Ear, Face, Head, and Neck)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e2) Minimal (n=489)	≤18.6	7.7 (65)	6.6 (121)	1.9 (54)	0.54 (0.28,1.06)	0.759 ^b 0.075 ^c
	>18.6	13.0 (54)	3.3 (121)	2.7 (74)	0.47 (0.24,0.92)	0.029 ^c
f2) Maximal (n=704)	≤18.6	5.9 (102)	8.4 (179)	1.2 (81)	0.76 (0.51,1.12)	0.941 ^b 0.166 ^c
	>18.6	3.8 (78)	7.2 (166)	2.0 (98)	0.74 (0.49,1.11)	0.143 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a		p-Value	Covariate Remarks	
g2) Minimal (n=476)	≤18.6	0.65 (0.33,1.29)		0.854 ^b 0.223 ^c	AGE (p=0.057) SUN2HR (p<0.001)	
	>18.6	0.60 (0.30,1.18)		0.140 ^c	ETHBACK (p=0.101)	
h2) Maximal (n=687)	≤18.6	0.86 (0.56,1.31)		0.954 ^b 0.479 ^c	AGE (p=0.017) SUN2HR (p<0.001)	
	>18.6	0.84 (0.54,1.32)		0.455 ^c	ETHBACK (p=0.076) LAT (p=0.078) HAIR (p=0.100)	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Trunk)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e3) Minimal (n=489)	≤18.6	6.2 (65)	2.5 (121)	3.7 (54)	0.66 (0.31,1.40)	0.872 ^b 0.277 ^c
	>18.6	5.6 (54)	0.8 (121)	2.7 (74)		
f3) Maximal (n=704)	≤18.6	2.9 (102)	3.9 (179)	2.5 (81)	0.92 (0.57,1.49)	0.927 ^b 0.738 ^c
	>18.6	1.3 (78)	2.4 (166)	2.0 (98)		

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g3) Minimal (n=489)	≤18.6	0.92 (0.42,2.00)	0.927 ^b 0.833 ^c	AGE (p=0.009) SUNRPT (p<0.001)
	>18.6	0.88 (0.42,1.84)	0.727 ^c	
h3) Maximal (n=704)	≤18.6	1.13 (0.67,1.91)	0.800 ^b 0.649 ^c	AGE (p=0.002) SUNRPT (p<0.001)
	>18.6	1.02 (0.58,1.81)	0.938 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Upper Extremities)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e4) Minimal (n=489)	≤18.6	0.0 (65)	0.8 (121)	0.0 (54)	--	--
	>18.6	1.9 (54)	0.0 (121)	1.4 (74)	1.05 (0.36,3.02)	0.929 ^c
f4) Maximal (n=704)	≤18.6	0.0 (102)	0.6 (179)	0.0 (81)	--	--
	>18.6	2.6 (78)	0.6 (166)	1.0 (98)	0.77 (0.35,1.72)	0.528 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g4) Minimal (n=489)	≤18.6	--	--	--
	>18.6	--	--	--
h4) Maximal (n=704)	≤18.6	--	--	SUN2HR (p=0.126)
	>18.6	0.76 (0.33,1.74)	0.516 ^c	

^aRelative risk for a twofold increase in dioxin.

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-8. (Continued)
Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Lower Extremities)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	<u>Percent Yes/(n)</u> <u>Current Dioxin</u>			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e5) Minimal (n=489)	≤18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f5) Maximal (n=704)	≤18.6	0.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.0 (166)	0.0 (98)	--	--
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
g5) Minimal (n=489)	≤18.6	--		--	--	
	>18.6	--		--	--	
h5) Maximal (n=704)	≤18.6	--		--	--	
	>18.6	--		--	--	

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-8. (Continued)
Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Other Sites and NOS)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e6) Minimal (n=489)	≤18.6	0.0 (65)	0.8 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	1.7 (121)	1.4 (74)	1.29 (0.59,2.86)	0.523 ^c
f6) Maximal (n=704)	≤18.6	0.0 (102)	0.6 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	1.2 (166)	1.0 (98)	1.52 (0.77,2.98)	0.224 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g6) Minimal (n=489)	≤18.6	--	--	SUN2HR (p=0.092)
	>18.6	1.32 (0.58,2.99)	0.509 ^c	
h6) Maximal (n=704)	≤18.6	--	--	SUN2HR (p=0.093)
	>18.6	1.57 (0.78,3.16)	0.209 ^c	

^aRelative risk for a twofold increase in dioxin.

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(All Sites Combined)
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	7.0	All Categories		0.101
Unknown	333	9.9	Unknown vs. Background	1.45 (0.92,2.30)	0.110
Low	184	9.2	Low vs. Background	1.34 (0.76,2.39)	0.313
High	179	4.5	High vs. Background	0.62 (0.29,1.33)	0.215
Total	1,435				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	718	All Categories		0.188	SUN2HR (p=0.008) LAT (p=0.023)
Unknown	324	Unknown vs. Background	1.45 (0.89,2.34)	0.134	AGE*ETHBACK
Low	180	Low vs. Background	1.51 (0.84,2.74)	0.171	(p=0.025)
High	175	High vs. Background	0.77 (0.35,1.69)	0.515	HAIR*XRAY (p=0.033) SUNRPT*XRAY (p=0.037)
Total	1,397				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Ear, Face, Head, and Neck)
(Verified)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	5.3	All Categories		0.026
Unknown	333	7.5	Unknown vs. Background	1.46 (0.87,2.45)	0.156
Low	184	6.0	Low vs. Background	1.14 (0.57,2.28)	0.707
High	179	1.7	High vs. Background	0.31 (0.09,1.00)	0.050
Total	1,435				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	718	All Categories		0.128	AGE (p=0.019) ETHBACK (p=0.018)
Unknown	324	Unknown vs. Background	1.34 (0.78,2.31)	0.285	HAIR (p=0.042)
Low	180	Low vs. Background	1.28 (0.63,2.59)	0.498	SUN2HR (p=0.022)
High	175	High vs. Background	0.38 (0.12,1.28)	0.119	SUNRPT (p=0.047) LAT (p=0.021)
Total	1,397				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Trunk)
(Verified)**

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	1.8	All Categories		0.955
Unknown	333	2.1	Unknown vs. Background	1.20 (0.47,3.04)	0.701
Low	184	1.6	Low vs. Background	0.93 (0.26,3.29)	0.904
High	179	2.2	High vs. Background	1.28 (0.41,3.97)	0.673
Total	1,435				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	738	All Categories		0.896	AGE (p=0.060) SUNRPT (p=0.009)
Unknown	333	Unknown vs. Background	1.21 (0.48,3.08)	0.689	
Low	184	Low vs. Background	0.97 (0.27,3.46)	0.961	
High	179	High vs. Background	1.53 (0.48,4.87)	0.468	
Total	1,434				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Upper Extremities)
(Verified)**

i4) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.5	All Categories		0.661
Unknown	333	1.2	Unknown vs. Background	2.23 (0.56,8.99)	0.426
Low	184	0.5	Low vs. Background	1.00 (0.11,9.04)	0.999
High	179	0.6	High vs. Background	1.03 (0.12,9.29)	0.999
Total	1,435				

j4) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	733	All Categories		0.735	HAIR (p=0.072) LAT (p=0.123)
Unknown	332	Unknown vs. Background	2.21 (0.54,9.01)	0.267	
Low	184	Low vs. Background	1.05 (0.12,9.49)	0.969	
High	179	High vs. Background	1.24 (0.14,11.38)	0.847	
Total	1,428				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Lower Extremities)**

i5) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.0	Unknown vs. Background	--	--
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j5) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

TABLE 7-8. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasms
(Other Sites and NOS)
(Verified)**

i6) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.1	All Categories		0.011
Unknown	333	0.0	Unknown vs. Background	--	0.999
Low	184	1.6	Low vs. Background	12.23 (1.27,118.3)	0.053
High	179	0.6	High vs. Background	4.15 (0.26,66.61)	0.704
Total	1,435				

j6) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		0.035	SUN2HR (p=0.070)
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	13.34 (1.40,127.1)	0.024	
High	179	High vs. Background	3.93 (0.25,62.34)	0.332	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.
 Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

not performed under the minimal assumption. Under the maximal assumption, the adjusted relative risk was nonsignificant (Table 7-8 [d4]: $p=0.889$).

No Ranch Hands had a verified sun exposure-related malignant skin neoplasm on the lower extremities (Table 7-8 [a5] and [b5]).

Four Ranch Hands had a verified sun exposure-related malignant neoplasm for other sites and sites NOS in these analyses. In the unadjusted analysis, the relative risks were greater than 1 but nonsignificant under both assumptions (Table 7-8 [a6] and [b6]: $p=0.469$ and $p=0.151$). Similarly, the adjusted analyses displayed nonsignificant relative risks (Table 7-8 [c6] and [d6]: $p=0.458$ and $p=0.143$).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified sun exposure-related malignant skin neoplasm for all sites combined displayed a nonsignificant current dioxin-by-time since tour interaction (Table 7-8 [e1]: $p=0.694$). For Ranch Hands with tours less than or equal to 18.6 years, the relative risk of a verified sun exposure-related malignant skin neoplasm was marginally significant (Est. $RR=0.63$, $p=0.065$) but less than 1. For that time stratum, the relative frequencies of Ranch Hands with a sun exposure-related malignant skin neoplasm for low, medium, and high current dioxin were 12.3, 9.9, and 5.6 percent. Under the maximal assumption, the interaction was nonsignificant (Table 7-8 [f1]: $p=0.910$). Under the minimal and maximal assumptions, the adjusted analyses contained nonsignificant interactions between current dioxin and time (Table 7-8 [g1] and [h1]: $p=0.452$ and $p=0.992$, respectively). Within strata analyses were also nonsignificant with relative risks consistently below 1.

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified sun exposure-related malignant skin neoplasm on the ear, face, head, and neck contained a nonsignificant interaction between current dioxin and time since tour (Table 7-8 [e2]: $p=0.759$); thus, the relative risks were not significantly different between time strata. For time less than or equal to 18.6 years, the relative risk was marginally significant (Est. $RR=0.54$, $p=0.075$) but less than 1. The relative frequencies of Ranch Hands within the low, medium, and high current dioxin categories were 7.7, 6.6, and 1.9 percent for that time stratum. For the other time stratum, the relative risk was significant but also less than 1 (Est. $RR=0.47$, $p=0.029$) and the associated relative frequencies of Ranch Hands were 13.0, 3.3, and 2.7 percent. Under the maximal assumption, the interaction of current dioxin and time since tour was nonsignificant (Table 7-8 [f2]: $p=0.941$) and the relative risks within time strata were nonsignificant and less than 1. Under both assumptions, the adjusted analyses exhibited nonsignificant interactions between current dioxin and time (Table 7-8 [g2] and [h2]: $p=0.854$ and $p=0.954$). Under the minimal assumption, after adjusting for age, skin reaction after at least 2 hours of sun exposure, and ethnic background, the relative risks of each time stratum became nonsignificant ($p=0.223$ and $p=0.140$).

Under both assumptions, the unadjusted analysis of the frequency of Ranch Hands with a verified sun exposure-related malignant skin neoplasm on the trunk displayed a nonsignificant interaction between current dioxin and time (Table 7-8 [e3] and [f3]: $p=0.872$

and $p=0.927$). The adjusted analyses also displayed nonsignificant current dioxin-by-time interactions (Table 7-8 [g3] and [h3]: $p=0.927$ and $p=0.800$).

Under the minimal assumption, three Ranch Hands had a verified sun exposure-related malignant skin neoplasm on the upper extremities (one Ranch Hand for time less than or equal to 18.6 years and two Ranch Hands for time over 18.6 years). Because only one Ranch Hand with a later tour had a verified sun exposure-related malignant skin neoplasm on the upper extremities, the relative risk, confidence interval, and p -value were not reported for that time stratum, as well as the p -value associated with the interaction of current dioxin and time. The relative risk for the other time stratum was nonsignificant (Table 7-8 [e4]: $p=0.929$). Under the maximal assumption, five Ranch Hands had a verified sun exposure-related malignant skin neoplasm on the upper extremities (one Ranch Hand for time less than or equal to 18.6 years and four Ranch Hands for time over 18.6 years). As in the minimal analysis, the interaction and relative risk for time less than or equal to 18.6 years were not evaluated because only one Ranch Hand had the neoplasm of interest in the later time since tour stratum. For time over 18.6 years, the relative risk was nonsignificant (Table 7-8 [f4]: $p=0.528$). An adjusted analysis was not performed under the minimal assumption due to sparse data. Under the maximal assumption, a nonsignificant relative risk was displayed for time over 18.6 years (Table 7-8 [h4]: $p=0.516$).

No Ranch Hands had a verified sun exposure-related malignant skin neoplasm on the lower extremities (Table 7-8 [e5] and [f5]).

Under both assumptions, one Ranch Hand in the time less than or equal to 18.6 years stratum and three Ranch Hands in the time over 18.6 years stratum had a verified sun exposure-related malignant skin neoplasm for other sites and sites NOS. The interaction of current dioxin and time since tour was not evaluated for significance nor was the relative risk for time less than or equal to 18.6 years due to the sparseness of these data. Under each assumption, the relative risk of sun exposure-related malignant skin neoplasms on other sites and NOS was nonsignificant (Table 7-8 [e6] and [f6]: $p=0.523$ and $p=0.224$) for time over 18.6 years. The adjusted analyses reported for time over 18.6 years displayed nonsignificant relative risks (Table 7-8 [g6] and [h6]: $p=0.509$ and $p=0.209$).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis for verified sun exposure-related malignant skin neoplasms for all sites combined, the relative frequencies were not significantly different among Ranch Hands with unknown, low, and high current dioxin and Comparisons with background current dioxin (Table 7-8 [i1]: $p=0.101$). There were no suspected cases of sun exposure-related malignant skin neoplasms. In the adjusted analysis, the overall contrast remained nonsignificant (Table 7-8 [j1]: $p=0.188$).

The unadjusted analysis of the frequencies of Ranch Hands and Comparisons with a verified sun exposure-related malignant skin neoplasm on the ear, face, head, and neck was significant (Table 7-8 [i2]: $p=0.026$). Among the Comparisons in the background current dioxin category, 5.3 percent of the participants had a verified sun exposure-related malignant skin neoplasm on the ear, face, head, and neck. The corresponding relative frequencies for Ranch Hands in the unknown, low, and high current dioxin categories were 7.5, 6.0, and 1.7

percent. The contrast of Ranch Hands in the high current dioxin category with Comparisons in the background category was significant but the risk was less than 1 (Est. RR=0.31, 95% C.I.: [0.09,1.00], p=0.050). The contrasts of low versus background (p=0.707) and unknown versus background (p=0.156) were both greater than 1 but nonsignificant. After adjusting for age, ethnic background, hair color, average lifetime residential latitude, and the two skin reaction to sun exposure covariates, the overall contrast became nonsignificant (Table 7-8 [j2]: p=0.128). Each of the Ranch Hand versus Comparison contrasts was also nonsignificant.

The unadjusted and the adjusted analyses for verified sun exposure-related malignant skin neoplasm on the trunk among Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category were nonsignificant (Table 7-8 [i3] and [j3]: p=0.955 and p=0.896, respectively).

Four Comparisons and six Ranch Hands (four in the unknown category, one in the low category, and one in the high category) had a verified sun exposure-related neoplasm on the upper extremities. The unadjusted analysis contrasting Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category contained a nonsignificant overall contrast (Table 7-8 [i4]: p=0.661). The overall contrast for the adjusted analysis was also nonsignificant (Table 7-8 [j4]: p=0.735).

No Comparisons and no Ranch Hands had a verified sun exposure-related malignant skin neoplasm on the lower extremities (Table 7-8 [i5]).

The unadjusted overall contrast of verified sun exposure-related malignant skin neoplasms for other sites and sites NOS among Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category was significant (Table 7-8 [i6]: p=0.011). The overall contrast was based on three Ranch Hands in the low category, one Ranch Hand in the high category, and one Comparison in the background category with these sun exposure-related malignant skin neoplasms. The corresponding relative frequencies for participants in the background, unknown, low, and high current dioxin categories were 0.1, 0.0, 1.6, and 0.6 percent. The contrast of low versus background was marginally significant (Est. RR=12.23, 95% C.I.: [1.27,118.3], p=0.053). The contrasts of unknown versus background and high versus background were nonsignificant (p=0.999 and p=0.704, respectively). Adjusting for skin reaction after at least 2 hours of sun exposure, the overall contrast remained significant (Table 7-8 [j6]: p=0.035). The low versus background contrast became significant in the adjusted analysis (Adj. RR=13.34, 95% C.I.: [1.40,127.1], p=0.024). The high versus background contrast was nonsignificant (p=0.332). In both of these analyses, the relative risks for the high versus background contrast was lower than that for the low versus background contrast.

Melanoma—All Sites and by Location/Site

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

There were only two Ranch Hands with verified melanoma in the minimal analysis, and consequently an unadjusted analysis was not performed. The unadjusted analysis under the maximal assumption was nonsignificant (Table 7-9 [b1]: p=0.223) based on only three

TABLE 7-9.

**Analysis of Melanoma
(All Sites Combined)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=489)	Low	118	1.7	--	--
	Medium	243	0.0		
	High	128	0.0		
b1) Maximal (n=704)	Low	181	0.0	0.52 (0.16,1.74)	0.223
	Medium	344	0.9		
	High	179	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c1) Minimal (n=489)	--		--	--	
d1) Maximal (n=704)	--		--	--	

^aRelative risk for a twofold increase in dioxin.

--: Analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-9. (Continued)
Analysis of Melanoma
(Ear, Face, Head, and Neck)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a2) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b2) Maximal (n=704)	Low	181	0.0	--	--
	Medium	344	0.3		
	High	179	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption			Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c2) Minimal (n=489)			--	--	--
d2) Maximal (n=704)			--	--	--

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Trunk)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a3) Minimal (n=489)	Low	118	1.7	0.01 (0.00,1.60)	0.011
	Medium	243	0.0		
	High	128	0.0		
b3) Maximal (n=704)	Low	181	0.0	0.52 (0.12,2.28)	0.315
	Medium	344	0.6		
	High	179	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c3) Minimal (n=489)	--		--	--	
d3) Maximal (n=704)	--		--	--	

^aRelative risk for a twofold increase in dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Upper Extremities)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a4) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b4) Maximal (n=704)	Low	181	0.0	--	--
	Medium	344	0.0		
	High	179	0.0		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c4) Minimal (n=489)	--	--	--
d4) Maximal (n=704)	--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Lower Extremities)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a5) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b5) Maximal (n=704)	Low	181	0.0	--	--
	Medium	344	0.0		
	High	179	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption			Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c5) Minimal (n=489)			--	--	--
d5) Maximal (n=704)			--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Other Sites and NOS)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a6) Minimal (n=489)	Low	118	0.0	--	--
	Medium	243	0.0		
	High	128	0.0		
b6) Maximal (n=704)	Low	181	0.0	--	--
	Medium	344	0.0		
	High	179	0.0		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c6) Minimal (n=489)	--	--	--
d6) Maximal (n=704)	--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(All Sites Combined)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=489)	≤18.6	1.5 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	1.9 (54)	0.0 (121)	0.0 (74)	--	--
f1) Maximal (n=704)	≤18.6	0.0 (102)	0.6 (179)	0.0 (81)	--	--
	>18.6	1.3 (78)	0.6 (166)	0.0 (98)	0.36 (0.06,2.31)	0.282 ^b

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted					
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks	
g1) Minimal (n=489)	≤18.6	--	--	--	
	>18.6	--	--	--	
h1) Maximal (n=704)	≤18.6	--	--	--	
	>18.6	--	--	--	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-9. (Continued)
Analysis of Melanoma
(Ear, Face, Head, and Neck)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e2) Minimal (n=489)	≤18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f2) Maximal (n=704)	≤18.6	0.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	1.3 (78)	0.0 (166)	0.0 (98)	--	--
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
g2) Minimal (n=489)	≤18.6	--		--	--	
	>18.6	--		--	--	
h2) Maximal (n=704)	≤18.6	--		--	--	
	>18.6	--		--	--	

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Trunk)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e3) Minimal (n=489)	≤18.6	1.5 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	1.9 (54)	0.0 (121)	0.0 (74)	--	--
f3) Maximal (n=704)	≤18.6	0.0 (102)	0.6 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.6 (166)	0.0 (98)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g3) Minimal (n=489)	≤18.6	--	--	--
	>18.6	--	--	--
h3) Maximal (n=704)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Upper Extremities)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e4) Minimal (n=489)	≤18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f4) Maximal (n=704)	≤18.6	0.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.0 (166)	0.0 (98)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g4) Minimal (n=489)	≤18.6	--	--	--
	>18.6	--	--	--
h4) Maximal (n=704)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Lower Extremities)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e5) Minimal (n=489)	≤18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f5) Maximal (n=704)	≤18.6	0.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.0 (166)	0.0 (98)	--	--
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks		
g5) Minimal (n=489)	≤18.6	--	--	--		
	>18.6	--	--	--		
h5) Maximal (n=704)	≤18.6	--	--	--		
	>18.6	--	--	--		

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Other Sites and NOS)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e6) Minimal (n=489)	≤18.6	0.0 (65)	0.0 (121)	0.0 (54)	--	--
	>18.6	0.0 (54)	0.0 (121)	0.0 (74)	--	--
f6) Maximal (n=704)	≤18.6	0.0 (102)	0.0 (179)	0.0 (81)	--	--
	>18.6	0.0 (78)	0.0 (166)	0.0 (98)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g6) Minimal (n=489)	≤18.6	--	--	--
	>18.6	--	--	--
h6) Maximal (n=704)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(All Sites Combined)
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.4	All Categories		--
Unknown	333	0.3	Unknown vs. Background	0.74 (0.08,7.13)	0.999
Low	184	0.0	Low vs. Background	--	0.999
High	179	0.0	High vs. Background	--	0.999
Total	1,435				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	738	All Categories		--	HAIR (p=0.076)
Unknown	333	Unknown vs. Background	0.64 (0.07,6.24)	0.702	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,434				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-9. (Continued)
Analysis of Melanoma
(Ear, Face, Head, and Neck)
(Verified)

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.3	Unknown vs. Background	--	0.622
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Trunk)
(Verified)**

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.4	All Categories		--
Unknown	333	0.0	Unknown vs. Background	--	0.654
Low	184	0.0	Low vs. Background	--	0.999
High	179	0.0	High vs. Background	--	0.999
Total	1,435				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.

Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.

Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.

High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Upper Extremities)
(Verified)**

i4) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.0	Unknown vs. Background	--	--
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j4) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Lower Extremities)
(Verified)**

i5) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.0	Unknown vs. Background	--	--
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j5) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-9. (Continued)

**Analysis of Melanoma
(Other Sites and NOS)
(Verified)**

i6) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.0	All Categories		--
Unknown	333	0.0	Unknown vs. Background	--	--
Low	184	0.0	Low vs. Background	--	--
High	179	0.0	High vs. Background	--	--
Total	1,435				

j6) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		--	--
Unknown	333	Unknown vs. Background	--	--	
Low	184	Low vs. Background	--	--	
High	179	High vs. Background	--	--	
Total	1,435				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

Ranch Hands with verified melanoma. Adjusted analyses were not performed due to the sparse number of Ranch Hands with melanoma.

Under the minimal assumption, no Ranch Hands had a verified melanoma on the ear, face, head, and neck (Table 7-9 [a2]). Under the maximal assumption, only one Ranch Hand had a verified melanoma on the ear, face, head, and neck (Table 7-9 [b2]). Because of the sparse number of Ranch Hands with melanoma on the ear, face, head, and neck, the relative risks, associated confidence intervals, and p-values of the unadjusted analyses were not presented and adjusted analyses were not performed.

Two Ranch Hands had verified melanoma on the trunk under both the minimal and the maximal assumptions. Under the minimal and maximal assumptions, different cutpoints were used to define the low, medium, and high initial categories (see the note at the bottom of Table 7-9 [a3-d3]). Therefore, the two Ranch Hands fell in the low initial dioxin category under the minimal assumption and fell in the medium initial dioxin category under the maximal assumption. Under the minimal assumption, the frequency of Ranch Hands with verified melanoma on the trunk was significant with a relative risk less than 1 (Table 7-9 [a3]: Est. RR=0.01, p=0.011) in the unadjusted analysis. Under the maximal assumption, the relative risk was nonsignificant (Table 7-9 [b3]: p=0.315). No adjusted analyses were performed due to the sparse number of participants with melanoma on the trunk.

No Ranch Hands had verified melanoma on the upper extremities (Table 7-9 [a4] and [b4]), on the lower extremities (Table 7-9 [a5] and [b5]), or for other sites and sites NOS (Table 7-9 [a6] and [b6]).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal assumption, two Ranch Hands had a verified melanoma for all sites combined (one Ranch Hand in each time since tour stratum). Due to the sparse number of melanoma within each time stratum, only relative frequencies and sample sizes are presented. Under the maximal assumption, three Ranch Hands had a verified melanoma for all sites combined (one Ranch Hand for time of 18.6 years or less and two Ranch Hands for time over 18.6 years). Because of the sparse number of Ranch Hands with melanoma within the former time stratum, neither the interaction nor the relative risk associated with the later time stratum was evaluated for significance. The estimated relative risk for the two Ranch Hands with tours over 18.6 years was nonsignificant (Table 7-9 [f1]: p=0.282). Adjusted analyses were not performed due to the sparse number of Ranch Hands with melanoma.

No Ranch Hands had a verified melanoma on the ear, face, head, and neck under the minimal assumption (Table 7-9 [e2]), and only one Ranch Hand had a verified melanoma under the maximal assumption (Table 7-9 [f2]). Due to these sparse numbers, only relative frequencies and sample sizes were presented. No analyses were performed.

Under each assumption, two Ranch Hands had a verified melanoma on the trunk (one in each time stratum). Due to the sparse number within each stratum, only relative frequencies and sample sizes were presented and no analyses were performed (Table 7-9 [e3-h3]).

As noted in the analysis using initial dioxin, no Ranch Hands had verified melanoma on the upper extremities (Table 7-9 [e4] and [f4]), on the lower extremities (Table 7-9 [e5] and [f5]), or for other sites and sites NOS (Table 7-9 [e6] and [f6]).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

Only three Comparisons and one Ranch Hand in the unknown current dioxin category had a verified melanoma for all sites combined (Table 7-9 [i1]). In the unadjusted analysis, none of the Ranch Hand versus Comparison contrasts was significant ($p=0.999$ for each contrast). An adjusted model containing hair color produced a nonsignificant unknown versus background contrast (Table 7-9 [j1]: $p=0.702$). Both relative risks were less than 1. There were no suspected cases of melanoma.

One Ranch Hand in the unknown current dioxin category had a verified melanoma on the ear, face, head, and neck (Table 7-9 [i2]). The unknown versus background contrast was nonsignificant in the unadjusted analysis ($p=0.622$). Due to the sparse number of Ranch Hands with a melanoma for this site, an adjusted analysis was not performed.

Three Comparisons, but no Ranch Hands (Table 7-9 [i3]), had a verified melanoma on the trunk. In the unadjusted analysis, each of the Ranch Hand versus Comparison contrasts was nonsignificant ($p>0.65$ for each contrast). An adjusted analysis was not performed because of the sparse number of Ranch Hands with a melanoma on the trunk.

No participants had a verified melanoma on the upper extremities (Table 7-9 [i4]), on the lower extremities (Table 7-9 [i5]), or for other sites and sites NOS (Table 7-9 [i6]).

Squamous Cell Carcinoma

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Three Ranch Hands had verified squamous cell carcinoma under each assumption. In the unadjusted analysis of the frequency of Ranch Hands with a squamous cell carcinoma, the relative risks for an association with initial dioxin were nonsignificant under both the minimal and maximal assumptions (Table 7-10 [a] and [b]: $p=0.836$ and $p=0.573$). Adjusted models containing only skin reaction after at least 2 hours of sun exposure produced nonsignificant results (Table 7-10 [c] and [d]: $p=0.860$ and $p=0.560$, respectively).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under each assumption, three Ranch Hands had a verified squamous cell carcinoma (two of the Ranch Hands had time since tour 18.6 years or less). Because only one Ranch Hand within the over 18.6 years time stratum had a squamous cell carcinoma, the relative risk for that time stratum and the interaction of current dioxin and time were not evaluated for significance. The estimated relative risk for the other time stratum was nonsignificant under the minimal and maximal assumptions (Table 7-10 [e] and [f]: $p=0.303$ and $p=0.804$). Because of the sparse nature of these data, no adjusted analyses were performed.

TABLE 7-10.
Analysis of Squamous Cell Carcinoma

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=489)	Low	118	0.8	0.90 (0.34,2.42)	0.836
	Medium	243	0.4		
	High	128	0.8		
b) Maximal (n=704)	Low	181	0.0	1.24 (0.60,2.60)	0.573
	Medium	344	0.6		
	High	179	0.6		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=489)	0.92 (0.34,2.48)	0.860	SUN2HR (p=0.109)
d) Maximal (n=704)	1.26 (0.59,2.72)	0.560	SUN2HR (p=0.104)

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal--** Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal-- Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-10. (Continued)
Analysis of Squamous Cell Carcinoma

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=489)						
	≤18.6	1.5 (65)	0.8 (121)	0.0 (54)	0.25 (0.02,3.48)	-- 0.303 ^b
	>18.6	0.0 (54)	0.0 (121)	1.4 (74)		
f) Maximal (n=704)						
	≤18.6	0.0 (102)	1.1 (179)	0.0 (81)	0.86 (0.26,2.86)	-- 0.804 ^b
	>18.6	0.0 (78)	0.0 (166)	1.0 (98)		
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
g) Minimal (n=489)						
	≤18.6	--		--	--	
	>18.6	--		--	--	
h) Maximal (n=704)						
	≤18.6	--		--	--	
	>18.6	--		--	--	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-10. (Continued)
Analysis of Squamous Cell Carcinoma
(Verified)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	739	0.1	All Categories		0.571
Unknown	333	0.6	Unknown vs. Background	4.46 (0.40,49.35)	0.458
Low	184	0.5	Low vs. Background	4.03 (0.25,64.78)	0.718
High	179	0.6	High vs. Background	4.15 (0.26,66.61)	0.704
Total	1,435				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	739	All Categories		0.546	SUN2HR (p=0.083)
Unknown	333	Unknown vs. Background	4.35 (0.40,47.57)	0.228	
Low	184	Low vs. Background	4.39 (0.28,69.66)	0.294	
High	179	High vs. Background	4.06 (0.26,64.37)	0.320	
Total	1,435				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis, there were only five participants with verified squamous cell carcinoma (one Comparison in the background category, two Ranch Hands in the unknown current dioxin category, one Ranch Hand in the low current dioxin category, and one Ranch Hand in the high current dioxin category). The overall contrast was nonsignificant (Table 7-10 [i]: $p=0.571$). An adjusted model containing only skin reaction after at least 2 hours of sun exposure also exhibited a nonsignificant overall contrast (Table 7-10 [j]: $p=0.546$).

Basal Cell Carcinoma on Specified Sites by Occupation

Analyses were performed by occupational stratum because the analyses were of special interest due to varying degrees of exposure resulting from different occupational duties. Occupation was not used routinely as a covariate for standard adjustment because of the known strong relationship between dioxin and occupation.

For these occupation-specific analyses of basal cell carcinoma, occupation and the interaction of occupation and dioxin were also included in the adjusted logistic regression model. These terms were added to the model to increase the sample size used to generate estimates and evaluate covariates. Common sets of covariates were reported (e.g., see Table 7-11 panels [c1], [c3], [c5]) because only one model was used to summarize results of each occupation for a specific analysis (e.g., basal cell carcinoma on the ear, face, head, and neck versus no basal cell carcinoma).

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

With respect to initial dioxin, under the minimal and the maximal assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand officers with a basal cell carcinoma on the ear, face, head, and neck versus Ranch Hand officers without basal cell carcinoma produced relative risks greater than 1; however, each of the risks was nonsignificant (Table 7-11 [a1-d1]: $p>0.35$ for all analyses).

Under the minimal assumption, there was only one Ranch Hand officer with a basal cell carcinoma of other sites; therefore, unadjusted and adjusted analyses were not performed. Under the maximal assumption, the unadjusted and the adjusted analyses of the frequency of Ranch Hand officers with a basal cell carcinoma for other sites versus Ranch Hand officers without basal cell carcinoma were nonsignificant with relative risks less than 1 (Table 7-11 [b2] and [d2]: $p=0.814$ and $p=0.783$, respectively).

Under the minimal and the maximal assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand enlisted flyers with a basal cell carcinoma on the ear, face, head, and neck versus Ranch Hand enlisted flyers without basal cell carcinoma produced nonsignificant relative risks that were less than 1 (Table 7-11 [a3-d3]: $p>0.10$ for all analyses).

Under both assumptions, the unadjusted analyses of the frequency of Ranch Hand enlisted flyers with a basal cell carcinoma for other sites versus Ranch Hand enlisted flyers without basal cell carcinoma were significant with relative risks greater than 2 (Table 7-11 [a4] and [b4]: Est. RR=2.28, $p=0.050$ and Est. RR=2.48, $p=0.015$). Under the minimal assumption, the relative frequency of Ranch Hand enlisted flyers with a basal cell carcinoma

TABLE 7-11.

**Analysis of Basal Cell Carcinoma by Occupation
(Officer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=105)	Low	61	8.2	1.15 (0.25,5.26)	0.860
	Medium	44	6.8		
	High	0	--		
b1) Maximal (n=237)	Low	113	6.2	1.41 (0.67,2.97)	0.372
	Medium	122	7.4		
	High	2	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c1) Minimal (n=102)	1.31 (0.27,6.47)		0.740	AGE (p=0.052) ETHBACK (p=0.113) SUN2HR (p=0.003)	
d1) Maximal (n=232)	1.25 (0.56,2.81)		0.581	AGE (p=0.032) ETHBACK (p=0.095) SUN2HR (p=0.001) HAIR (p=0.149)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Officer—Other Sites versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a2) Minimal (n=98)	Low	56	0.0	--	--
	Medium	42	2.4		
	High	0	--		
b2) Maximal (n=228)	Low	111	4.5	0.87 (0.27,2.78)	0.814
	Medium	115	1.7		
	High	2	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c2) Minimal (n=98)	--		--	--	
d2) Maximal (n=228)	0.85 (0.26,2.76)		0.783	SUNRPT (p=0.010)	

^aRelative risk for a twofold increase in dioxin.

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Flyer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a3) Minimal (n=98)	Low	20	15.0	0.55 (0.17,1.82)	0.290
	Medium	59	1.7		
	High	19	5.3		
b3) Maximal (n=122)	Low	20	10.0	0.58 (0.27,1.24)	0.138
	Medium	71	5.6		
	High	31	3.2		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c3) Minimal (n=94)	0.62 (0.19,2.01)		0.426	AGE (p=0.052) ETHBACK (p=0.113) SUN2HR (p=0.003)	
d3) Maximal (n=116)	0.52 (0.23,1.16)		0.112	AGE (p=0.032) ETHBACK (p=0.095) SUN2HR (p=0.001) HAIR (p=0.149)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Flyer—Other Sites versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a4) Minimal (n=99)	Low	18	5.6	2.28 (0.98,5.33)	0.050
	Medium	59	1.7		
	High	22	18.2		
b4) Maximal (n=121)	Low	18	0.0	2.48 (1.13,5.44)	0.015
	Medium	69	2.9		
	High	34	11.8		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c4) Minimal (n=99)	1.97 (0.86,4.49)		0.108	SUNRPT (p=0.003)	
d4) Maximal (n=121)	2.22 (1.04,4.74)		0.039	SUNRPT (p=0.010)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Groundcrew—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a5) Minimal (n=272)	Low	34	5.9	0.43 (0.22,0.84)	0.005
	Medium	134	6.0		
	High	104	1.0		
b5) Maximal (n=325)	Low	43	2.3	0.65 (0.41,1.03)	0.051
	Medium	142	6.3		
	High	140	1.4		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c5) Minimal (n=266)	0.43 (0.21,0.88)		0.021	AGE (p=0.052) ETHBACK (p=0.113) SUN2HR (p=0.003)	
d5) Maximal (n=319)	0.67 (0.41,1.09)		0.104	AGE (p=0.032) ETHBACK (p=0.095) SUN2HR (p=0.001) HAIR (p=0.149)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Groundcrew—Other Sites versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a6) Minimal (n=268)	Low	34	5.9	0.56 (0.27,1.18)	0.096
	Medium	130	3.1		
	High	104	1.0		
b6) Maximal (n=320)	Low	42	0.0	0.83 (0.49,1.43)	0.501
	Medium	138	3.6		
	High	140	1.4		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c6) Minimal (n=268)	0.56 (0.25,1.29)		0.175	SUNRPT (p=0.003)	
d6) Maximal (n=320)	0.83 (0.49,1.42)		0.498	SUNRPT (p=0.010)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Officer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=105)	≤18.6	6.1 (33)	0.0 (14)	-- (0)	0.33 (0.00,39.39)	0.787 ^b 0.649 ^c
	>18.6	12.5 (32)	7.7 (26)	-- (0)	0.66 (0.08,5.86)	0.712 ^c
f1) Maximal (n=237)	≤18.6	4.5 (66)	6.9 (58)	0.0 (1)	1.27 (0.35,4.57)	0.889 ^b 0.719 ^c
	>18.6	4.3 (46)	10.8 (65)	0.0 (1)	1.43 (0.48,4.26)	0.524 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a		p-Value	Covariate Remarks	
g1) Minimal (n=102)	≤18.6	0.32 (0.00,43.41)		0.767 ^b 0.647 ^c	AGE (p=0.088) ETHBACK (p=0.088)	
	>18.6	0.69 (0.07,6.71)		0.751 ^c	SUN2HR (p=0.003)	
h1) Maximal (n=232)	≤18.6	1.20 (0.31,4.65)		0.947 ^b 0.796 ^c	AGE (p=0.008) ETHBACK (p=0.065)	
	>18.6	1.27 (0.37,4.42)		0.705 ^c	SUN2HR (p=0.008) SUNRPT (p=0.103)	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Officer—Other Sites versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e2) Minimal (n=98)	≤18.6	0.0 (31)	0.0 (14)	-- (0)	--	--
	>18.6	0.0 (28)	4.0 (25)	-- (0)	--	--
f2) Maximal (n=228)	≤18.6	4.5 (66)	0.0 (54)	0.0 (1)	0.31 (0.02,4.26)	0.623 ^b 0.380 ^c
	>18.6	6.4 (47)	1.7 (59)	0.0 (1)	0.67 (0.12,3.77)	0.648 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g2) Minimal (n=98)	≤18.6	--	--	--
	>18.6	--	--	--
h2) Maximal (n=228)	≤18.6	0.26 (0.02,4.10)	0.542 ^b 0.337 ^c	SUNRPT (p=0.011)
	>18.6	0.69 (0.12,3.89)	0.676 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Flyer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e3) Minimal (n=98)	≤18.6	12.5 (8)	5.9 (34)	20.0 (5)	1.08 (0.34,3.42)	0.891 ^c
	>18.6	12.5 (8)	0.0 (33)	0.0 (10)	--	--
f3) Maximal (n=122)	≤18.6	14.3 (14)	8.6 (35)	7.1 (14)	0.82 (0.36,1.85)	0.630 ^c
	>18.6	0.0 (7)	2.7 (37)	0.0 (15)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g3) Minimal (n=94)	≤18.6	1.35 (0.41,4.46)	0.624 ^c	AGE (p=0.088) ETHBACK (p=0.088)
	>18.6	--	--	SUN2HR (p=0.003)
h3) Maximal (n=116)	≤18.6	0.63 (0.24,1.65)	0.352 ^c	AGE (p=0.008) ETHBACK (p=0.065)
	>18.6	--	--	SUN2HR (p=0.008) SUNRPT (p=0.103)

^aRelative risk for a twofold increase in dioxin.

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Flyer—Other Sites versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e4) Minimal (n=99)	≤18.6	12.5 (8)	3.0 (33)	20.0 (5)	1.05 (0.26,4.25)	0.011 ^b 0.944 ^c
	>18.6	0.0 (7)	0.0 (33)	23.1 (13)	29.35 (1.23,702.4)	0.037 ^c
f4) Maximal (n=121)	≤18.6	0.0 (12)	5.9 (34)	7.1 (14)	1.49 (0.52,4.26)	0.017 ^b 0.457 ^c
	>18.6	0.0 (7)	0.0 (36)	16.7 (18)	29.37 (1.22,708.2)	0.037 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a		p-Value	Covariate Remarks	
g4) Minimal (n=99)	≤18.6	1.19 (0.34,4.20)		0.017 ^b 0.781 ^c	SUNRPT (p=0.005)	
	>18.6	37.64 (0.92, 1,541.9)		0.055 ^c		
h4) Maximal (n=121)	≤18.6	1.60 (0.60,4.27)		0.027 ^b 0.348 ^c	SUNRPT (p=0.011)	
	>18.6	37.64 (0.92, 1,543.3)		0.056 ^c		

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Groundcrew—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e5) Minimal (n=272)	≤18.6	4.5 (22)	7.2 (69)	0.0 (47)	0.30 (0.09,1.01)	0.901 ^b 0.051 ^c
	>18.6	14.3 (14)	3.4 (59)	1.6 (61)	0.33 (0.11,0.98)	0.047 ^c
f5) Maximal (n=325)	≤18.6	5.3 (19)	7.5 (80)	0.0 (64)	0.53 (0.26,1.09)	0.581 ^b 0.086 ^c
	>18.6	0.0 (22)	6.6 (61)	1.3 (79)	0.70 (0.37,1.31)	0.265 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g5) Minimal (n=266)	≤18.6	0.31 (0.09,1.10)	0.714 ^b 0.069 ^c	AGE (p=0.088) ETHBACK (p=0.088)
	>18.6	0.42 (0.15,1.20)	0.107 ^c	SUN2HR (p=0.003)
h5) Maximal (n=319)	≤18.6	0.51 (0.23,1.12)	0.385 ^b 0.092 ^c	AGE (p=0.008) ETHBACK (p=0.065)
	>18.6	0.80 (0.42,1.53)	0.492 ^c	SUN2HR (p=0.008) SUNRPT (p=0.103)

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Groundcrew—Other Sites versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)^a	p-Value
		Low	Medium	High		
e6) Minimal						0.980^b
(n=268)	≤18.6	4.5 (22)	4.5 (67)	2.1 (48)	0.61 (0.24,1.58)	0.313 ^c
	>18.6	0.0 (12)	3.4 (59)	0.0 (60)	0.60 (0.17,2.17)	0.438 ^c
f6) Maximal						0.989^b
(n=320)	≤18.6	0.0 (18)	5.1 (78)	1.5 (65)	0.90 (0.44,1.82)	0.759 ^c
	>18.6	0.0 (22)	3.4 (59)	0.0 (78)	0.90 (0.37,2.21)	0.823 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
g6) Minimal						
(n=268)	≤18.6	0.61 (0.23,1.58)		0.976 ^b	SUNRPT (p=0.005)	
	>18.6	0.62 (0.18,2.13)		0.305 ^c		
				0.448 ^c		
h6) Maximal						
(n=320)	≤18.6	0.85 (0.42,1.74)		0.874 ^b	SUNRPT (p=0.011)	
	>18.6	0.94 (0.39,2.25)		0.666 ^c		
				0.883 ^c		

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Officer—Ear, Face, Head, and Neck versus None)
(Verified)**

ii) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	275	6.2	All Categories		0.912
Unknown	202	7.4	Unknown vs. Background	1.22 (0.59,2.50)	0.720
Low	37	5.4	Low vs. Background	0.87 (0.19,3.93)	0.999
High	2	0.0	High vs. Background	--	0.999
Total	516				

ji) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	268	All Categories		0.865	AGE (p=0.032) ETHBACK (p=0.026)
Unknown	199	Unknown vs. Background	1.13 (0.52,2.44)	0.757	SUN2HR (p=0.028)
Low	36	Low vs. Background	0.75 (0.15,3.66)	0.719	SUNRPT (p=0.039)
High	2	High vs. Background	--	--	LAT (p=0.036) HAIR (p=0.085)
Total	505				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Officer—Other Sites versus None)
(Verified)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	262	1.5	All Categories		0.398
Unknown	195	4.1	Unknown vs. Background	2.76 (0.82,9.33)	0.161
Low	36	2.8	Low vs. Background	1.84 (0.20,16.96)	0.954
High	2	0.0	High vs. Background	--	0.999
Total	495				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	261	All Categories		0.356	SUNRPT (p=0.003)
Unknown	195	Unknown vs. Background	2.89 (0.85,9.81)	0.087	
Low	36	Low vs. Background	1.91 (0.21,17.70)	0.569	
High	2	High vs. Background	--	--	
Total	494				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Flyer—Ear, Face, Head, and Neck versus None)
(Verified)**

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	115	7.0	All Categories		0.530
Unknown	39	7.7	Unknown vs. Background	1.11 (0.28,4.46)	0.999
Low	50	2.0	Low vs. Background	0.27 (0.03,2.27)	0.366
High	29	3.4	High vs. Background	0.48 (0.06,4.03)	0.850
Total	233				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	110	All Categories		0.481	AGE (p=0.032)
Unknown	36	Unknown vs. Background	1.72 (0.39,7.65)	0.472	ETHBACK (p=0.026)
Low	49	Low vs. Background	0.37 (0.04,3.19)	0.358	SUN2HR (p=0.028)
High	28	High vs. Background	0.45 (0.05,4.09)	0.472	SUNRPT (p=0.039)
Total	223				LAT (p=0.036) HAIR (p=0.085)

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Flyer—Other Sites versus None)
(Verified)**

i4) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	108	0.9	All Categories		0.003
Unknown	36	0.0	Unknown vs. Background	--	0.999
Low	50	2.0	Low vs. Background	2.18 (0.13,36.20)	0.999
High	32	12.5	High vs. Background	15.29 (1.62,144.2)	0.020
Total	226				

j4) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	108	All Categories		0.028	SUNRPT (p=0.003)
Unknown	36	Unknown vs. Background	--	--	
Low	50	Low vs. Background	2.56 (0.15,42.6)	0.511	
High	32	High vs. Background	15.44 (1.59,147.1)	0.017	
Total	226				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Groundcrew—Ear, Face, Head, and Neck versus None)
(Verified)**

i5) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	338	3.8	All Categories		0.052
Unknown	84	4.8	Unknown vs. Background	1.25 (0.40,3.94)	0.703
Low	91	7.7	Low vs. Background	2.08 (0.81,5.39)	0.131
High	143	0.7	High vs. Background	0.18 (0.02,1.36)	0.095
Total	656				

j5) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	329	All Categories		0.048	AGE (p=0.032) ETHBACK (p=0.026)
Unknown	81	Unknown vs. Background	1.23 (0.38,4.04)	0.734	SUN2HR (p=0.028)
Low	89	Low vs. Background	2.22 (0.84,5.91)	0.110	SUNRPT (p=0.039)
High	140	High vs. Background	0.20 (0.03,1.55)	0.121	LAT (p=0.036) HAIR (p=0.085)
Total	639				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-11. (Continued)

**Analysis of Basal Cell Carcinoma by Occupation
(Enlisted Groundcrew—Other Sites versus None)
(Verified)**

i6) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	331	1.8	All Categories		0.091
Unknown	80	0.0	Unknown vs. Background	--	0.540
Low	88	4.5	Low vs. Background	2.58 (0.71,9.37)	0.274
High	143	0.7	High vs. Background	0.38 (0.05,3.21)	0.648
Total	642				

j6) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	331	All Categories		0.081	SUNRPT (p=0.003)
Unknown	80	Unknown vs. Background	--	--	
Low	88	Low vs. Background	2.47 (0.67,9.08)	0.171	
High	143	High vs. Background	0.37 (0.04,3.09)	0.354	
Total	642				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.

Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.

Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.

High (Ranch Hands): Current Dioxin >33.3 ppt.

on other sites were 5.6, 1.7 and 18.2 percent for low, medium, and high initial dioxin. Under the maximal assumption, the corresponding frequencies were 0.0, 2.9, and 11.8 percent. Under the minimal assumption, an adjusted model containing skin reaction after repeated sun exposure produced an adjusted relative risk for Ranch Hand enlisted flyers that was nonsignificant (Table 7-11 [c4]: $p=0.108$). Under the maximal assumption, the adjusted relative risk was significant and remained greater than 2 (Table 7-11 [d4]: Adj. RR=2.22, $p=0.039$). These results contrast with the nonsignificant relative risks less than 1 in the other occupational strata.

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted groundcrew with a basal cell carcinoma on the ear, face, head, and neck versus Ranch Hand enlisted groundcrew without basal cell carcinoma produced a relative risk that was significant but less than 1 (Table 7-11 [a5]: Est. RR=0.43, $p=0.005$). The relative frequencies of Ranch Hands within the low, medium, and high initial dioxin categories were 5.9, 6.0, and 1.0 percent. Under the maximal assumption, the unadjusted analysis produced a marginally significant relative risk that also was less than 1 (Table 7-11 [b5]: Est. RR=0.65, $p=0.051$). The corresponding relative frequencies for this analysis were 2.3, 6.3, and 1.4 percent for low, medium, and high initial dioxin. After adjusting for covariates, the relative risk under the minimal assumption remained significant and less than 1 (Table 7-11 [c5]: Adj. RR=0.43, $p=0.021$). Under the maximal assumption after adjusting for age, ethnic background, skin reaction after at least 2 hours of sun exposure, and hair color, the relative risk became nonsignificant (Table 7-11 [d5]: $p=0.104$) but remained less than 1.

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted groundcrew with a basal cell carcinoma for other sites versus Ranch Hand enlisted groundcrew without basal cell carcinoma were marginally significant with a relative risk less than 1 (Table 7-11 [a6]: Est. RR=0.56, $p=0.096$) with relative frequencies of Ranch Hand enlisted groundcrew being 5.9, 3.1, and 1.0 percent for low, medium, and high initial dioxin. Under the maximal assumption, the relative risk was less than 1 and nonsignificant (Table 7-11 [b6]: $p=0.501$). After adjusting for skin reaction to repeated sun exposure, the relative risks for Ranch Hand enlisted groundcrew with a basal cell carcinoma for other sites were also nonsignificant (Table 7-11 [c6] and [d6]: $p=0.175$ and $p=0.498$) under each assumption.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under both assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand officers with a basal cell carcinoma on the ear, face, head, and neck versus Ranch Hand officers without basal cell carcinoma exhibited nonsignificant interactions between current dioxin and time since tour (Table 7-11 [e1-h1]: $p>0.75$ for each interaction). Although nonsignificant, the relative risks for the individual time stratum were less than 1 under the minimal assumption and greater than 1 under the maximal assumption.

Under the minimal assumption, neither the unadjusted nor the adjusted analysis of the frequency of Ranch Hand officers with a basal cell carcinoma for other sites versus Ranch Hand officers without basal cell carcinoma was performed because only one Ranch Hand officer had the neoplasm of interest. Under the maximal assumption, the unadjusted and the adjusted analyses contained nonsignificant current dioxin-by-time interactions (Table 7-11 [f2] and [h2]: $p=0.623$ and $p=0.542$, respectively) and nonsignificant relative risks less than 1 within each time stratum.

Under both assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand enlisted flyers with a basal cell carcinoma on the ear, face, head, and neck versus Ranch Hand enlisted flyers without basal cell carcinoma were limited to the later tour stratum (18.6 years or less) because of the sparse number of Ranch Hands with the neoplasm of interest who served in Vietnam in the earlier time period. Under each assumption and for each analysis, the relative risks were nonsignificant (Table 7-11 [e3-h3]: $p > 0.35$ for each analysis). The unadjusted and adjusted relative risks were greater than 1 under the minimal assumption and less than 1 under the maximal assumption.

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted flyers with a basal cell carcinoma for other sites versus Ranch Hand enlisted flyers without a basal cell carcinoma contained a significant interaction between current dioxin and time (Table 7-11 [e4]: $p = 0.011$). Ranch Hand enlisted flyers with the later tours (18.6 years or less) displayed a nonsignificant relative risk greater than 1 ($p = 0.944$) and a significant relative risk greater than 1 was found for Ranch Hands within the other time stratum (Est. RR=29.35, $p = 0.037$). The relative frequencies of Ranch Hand enlisted flyers for the earlier tour stratum were 0.0, 0.0, and 23.1 percent for low, medium, and high current dioxin. Under the maximal assumption, the current dioxin-by-time interaction of the unadjusted analysis was also significant (Table 7-11 [f4]: $p = 0.017$) with a nonsignificant relative risk greater than 1 for Ranch Hands with later tours ($p = 0.457$) and a significant relative risk greater than 1 for Ranch Hands with earlier tours (Est. RR=29.37, $p = 0.037$). The corresponding relative frequencies of Ranch Hand enlisted flyers within the earlier tour stratum were 0.0, 0.0, and 16.7 percent. After adjusting for skin reaction after repeated sun exposure, significant interactions between current dioxin and time (Table 7-11 [g4] and [h4]: $p = 0.017$ and $p = 0.027$) and marginally significant relative risks greater than 1 for the enlisted flyers with earlier tours (minimal, Adj. RR=37.64, $p = 0.055$; maximal, Adj. RR=37.64, $p = 0.056$) were found in the adjusted analyses. Ranch Hands with later tours displayed nonsignificant relative risks. In the unadjusted and adjusted analyses, the significant or marginally significant associations found for Ranch Hands with early tours were based on three Ranch Hands in the high current dioxin category.

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted groundcrew with a basal cell carcinoma on the ear, face, head, and neck versus Ranch Hand enlisted groundcrew without a basal cell carcinoma contained a nonsignificant interaction between current dioxin and time (Table 7-11 [e5]: $p = 0.901$). However, for time of 18.6 years or less, the relative risk was marginally significant (Est. RR=0.30, $p = 0.051$) but less than 1; for time over 18.6 years the relative risk was significant (Est. RR=0.33, $p = 0.047$) but also less than 1. Relative frequencies of Ranch Hand enlisted groundcrew within the low, medium, and high current dioxin categories were 4.5, 7.2, and 0.0 percent for the later tour stratum and 14.3, 3.4, and 1.6 percent for the earlier tour stratum. Under the maximal assumption, the unadjusted analysis also contained a nonsignificant interaction between current dioxin and time (Table 7-11 [f5]: $p = 0.581$). Within the later tour stratum, the relative risk was marginally significant but less than 1 (Est. RR=0.53, $p = 0.086$) with associated relative frequencies of Ranch Hand enlisted groundcrew being 5.3, 7.5, and 0.0 percent for low, medium, and high current dioxin. Under both assumptions, the adjusted analyses displayed nonsignificant interactions (Table 7-11 [g5] and [h5]: $p = 0.714$ and $p = 0.385$). For both assumptions, however, the later time stratum contained marginally significant relative risks that were less than 1 (minimal, Adj. RR=0.31, $p = 0.069$; maximal, Adj. RR=0.51, $p = 0.092$).

Under each assumption, the unadjusted and adjusted analyses of the frequency of Ranch Hand enlisted groundcrew with a basal cell carcinoma for other sites versus Ranch Hand enlisted groundcrew without a basal cell carcinoma contained nonsignificant interactions between current dioxin and time (Table 7-11 [e6-h6]: $p > 0.85$ for each interaction).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The frequencies of study participants with a basal cell carcinoma on the ear, face, head, and neck versus the frequencies of study participants without a basal cell carcinoma were compared for Ranch Hand officers in the unknown, low, and high current dioxin categories and Comparison officers in the background category. The sample sizes and frequencies for Ranch Hands in the low and high categories were small. The unadjusted analysis contained a nonsignificant overall contrast (Table 7-11 [i1]: $p = 0.912$). The corresponding adjusted analysis also resulted in a nonsignificant overall contrast (Table 7-11 [j1]: $p = 0.865$). All Ranch Hand versus Comparison contrasts that were performed were also nonsignificant.

Study participants with a basal cell carcinoma for other sites versus study participants without a basal cell carcinoma were compared for Ranch Hand officers in the unknown, low, and high current dioxin categories and Comparison officers in the background category. The unadjusted analysis contained a nonsignificant overall contrast (Table 7-11 [i2]: $p = 0.398$). Individual Ranch Hand versus Comparison contrasts were nonsignificant. The adjusted analysis also exhibited a nonsignificant overall contrast (Table 7-11 [j2]: $p = 0.356$); however, after adjusting for skin reaction after repeated sun exposure, the low versus background contrast became marginally significant (Est. RR=2.89, 95% C.I.: [0.85, 9.81], $p = 0.087$).

The frequencies of study participants with a basal cell carcinoma on the ear, face, head, and neck versus the frequencies of study participants without a basal cell carcinoma were compared for Ranch Hand enlisted flyers in the unknown, low, and high current dioxin categories and Comparison enlisted flyers in the background category. The unadjusted and adjusted analyses contained nonsignificant overall contrasts (Table 7-11 [i3] and [j3]: $p = 0.530$ and $p = 0.481$, respectively). None of the Ranch Hand versus Comparison contrasts was significant.

Study participants with a basal cell carcinoma for other sites versus study participants without a basal cell carcinoma were compared for Ranch Hand enlisted flyers in the unknown, low, and high current dioxin categories and Comparison enlisted flyers in the background category. The unadjusted analysis contained a significant overall contrast (Table 7-11 [i4]: $p = 0.003$). The relative frequencies for the background, unknown, low, and high current dioxin categories were 0.9, 0.0, 2.0, and 12.5 percent. The high versus background contrast was significant (Est. RR=15.29, 95% C.I.: [1.62, 144.2], $p = 0.020$). The unknown versus background and the low versus background contrasts were nonsignificant ($p = 0.999$ for both contrasts). The adjusted analysis also displayed a significant overall contrast (Table 7-11 [j4]: $p = 0.028$) with the high versus background contrast being significant (Adj. RR=15.44, 95% C.I.: [1.59, 147.1], $p = 0.017$). The low versus background contrast was nonsignificant ($p = 0.511$).

The frequencies of study participants with a basal cell carcinoma on the ear, face, head, and neck versus the frequencies of study participants without a basal cell carcinoma were

compared for Ranch Hand enlisted groundcrew in the unknown, low, and high current dioxin categories and for Comparison enlisted groundcrew in the background category. The unadjusted analysis contained a marginally significant overall contrast (Table 7-11 [i5]: $p=0.052$). The relative frequencies for the background, unknown, low, and high current dioxin categories were 3.8, 4.8, 7.7, and 0.7 percent. The high versus background contrast was also marginally significant but the relative risk was less than 1 (Est. RR=0.18, 95% C.I.: [0.02,1.36], $p=0.095$). The unknown versus background and the low versus background contrasts were nonsignificant ($p=0.703$ and $p=0.131$, respectively). After adjustment for age, ethnic background, the two skin reaction covariates, average lifetime residential latitude, and hair color, the overall contrast became significant (Table 7-11 [j5]: $p=0.048$); however, each of the individual contrasts of interest was nonsignificant ($p>0.10$ for each contrast).

Study participants with a basal cell carcinoma for other sites versus study participants without a basal cell carcinoma were compared for Ranch Hand enlisted groundcrew in the unknown, low, and high current dioxin categories and for Comparison enlisted groundcrew in the background category. The unadjusted analysis contained a marginally significant overall contrast (Table 7-11 [i6]: $p=0.091$). The relative frequencies for the background, unknown, low, and high current dioxin categories were 1.8, 0.0, 4.5, and 0.7 percent. None of the individual contrasts of interest was significant ($p>0.25$ for all contrasts). The adjusted analysis also contained a marginally significant overall contrast (Table 7-11 [j6]: $p=0.081$) accompanied by nonsignificant individual contrasts.

Sun Exposure-Related Malignant Skin Neoplasms on Specified Sites by Occupation

Similar to the analyses of basal cell carcinoma by occupation, the logistic regression model was expanded to contain occupation and a dioxin-by-occupation interaction for the adjusted analyses of sun exposure-related malignant skin neoplasms by occupation. As stated earlier, the additional terms were placed in the model to increase the sample size used to generate parameter estimates and to evaluate covariates. Because only one model was used for determining parameter estimates for each occupation, the same covariates and their associated p -values were reported for each occupation.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

With respect to initial dioxin under the minimal and the maximal assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand officers with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus Ranch Hand officers without a sun exposure-related malignant skin neoplasm produced nonsignificant relative risks (Table 7-12 [a1-d1]: $p>0.35$ for all analyses).

Under both assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand officers with a sun exposure-related malignant skin neoplasm on other sites versus Ranch Hand officers without a sun exposure-related malignant skin neoplasm produced nonsignificant relative risks that were less than 1 (Table 7-12 [a2-d2]: $p\geq 0.70$ for all analyses).

Under the minimal and the maximal assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand enlisted flyers with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus Ranch Hand enlisted flyers

TABLE 7-12.

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Officer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=103)	Low	59	10.2	0.83 (0.18,3.80)	0.804
	Medium	44	6.8		
	High	0	--		
b1) Maximal (n=235)	Low	113	6.2	1.40 (0.69,2.83)	0.355
	Medium	120	9.2		
	High	2	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c1) Minimal (n=100)	0.82 (0.16,4.26)		0.813	AGE (p=0.030) ETHBACK (p=0.082) SUN2HR (p<0.001)	
d1) Maximal (n=230)	1.20 (0.56,2.57)		0.631	AGE (p=0.019) ETHBACK (p=0.075) SUN2HR (p<0.001) LAT (p=0.085) HAIR (p=0.063)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Officer—Other Sites versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a2) Minimal (n=97)	Low	55	3.6	0.61 (0.04,8.63)	0.700
	Medium	42	2.4		
	High	0	--		
b2) Maximal (n=226)	Low	111	4.5	0.90 (0.32,2.49)	0.833
	Medium	113	3.5		
	High	2	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c2) Minimal (n=97)	0.65 (0.05,9.10)		0.746	SUNRPT (p<0.001)	
d2) Maximal (n=226)	0.89 (0.32,2.52)		0.830	SUNRPT (p=0.002)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Flyer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a3) Minimal (n=98)	Low	20	15.0	0.54 (0.18,1.63)	0.233
	Medium	59	3.4		
	High	19	5.3		
b3) Maximal (n=122)	Low	20	10.0	0.62 (0.30,1.25)	0.157
	Medium	71	7.0		
	High	31	3.2		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c3) Minimal (n=94)	0.61 (0.21,1.77)		0.364	AGE (p=0.030) ETHBACK (p=0.082) SUN2HR (p<0.001)	
d3) Maximal (n=116)	0.54 (0.26,1.13)		0.101	AGE (p=0.019) ETHBACK (p=0.075) SUN2HR (p<0.001) LAT (p=0.085) HAIR (p=0.063)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal-- Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal-- Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Flyer—Other Sites versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a4) Minimal (n=98)	Low	18	5.6	2.27 (0.97,5.30)	0.052
	Medium	58	1.7		
	High	22	18.2		
b4) Maximal (n=120)	Low	18	0.0	2.47 (1.13,5.42)	0.015
	Medium	68	2.9		
	High	34	11.8		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c4) Minimal (n=98)	1.89 (0.83,4.30)		0.128	SUNRPT (p<0.001)	
d4) Maximal (n=120)	2.14 (1.00,4.54)		0.049	SUNRPT (p=0.002)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**-- Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal-- Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Groundcrew—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a5) Minimal (n=272)	Low	34	5.9	0.54 (0.30,0.97)	0.022
	Medium	134	6.0		
	High	104	1.9		
b5) Maximal (n=325)	Low	43	2.3	0.73 (0.48,1.12)	0.133
	Medium	142	6.3		
	High	140	2.1		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c5) Minimal (n=266)	0.56 (0.30,1.03)		0.063	AGE (p=0.030) ETHBACK (p=0.082) SUN2HR (p<0.001)	
d5) Maximal (n=319)	0.77 (0.49,1.22)		0.265	AGE (p=0.019) ETHBACK (p=0.075) SUN2HR (p<0.001) LAT (p=0.085) HAIR (p=0.063)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal-- Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal-- Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Groundcrew—Other Sites versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a6) Minimal (n=267)	Low	34	5.9	0.57 (0.27,1.18)	0.098
	Medium	130	3.1		
	High	103	1.0		
b6) Maximal (n=319)	Low	42	0.0	0.84 (0.49,1.44)	0.507
	Medium	138	3.6		
	High	139	1.4		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c6) Minimal (n=267)	0.56 (0.28,1.13)		0.104	SUNRPT (p<0.001)	
d6) Maximal (n=319)	0.83 (0.49,1.41)		0.485	SUNRPT (p=0.002)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal-- Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal-- Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Officer—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=103)	≤18.6	9.4 (32)	0.0 (14)	-- (0)	0.25 (0.00,16.43)	0.698 ^b 0.514 ^c
	>18.6	12.9 (31)	7.7 (26)	-- (0)	0.61 (0.07,5.56)	0.662 ^c
f1) Maximal (n=235)	≤18.6	4.5 (66)	8.8 (57)	0.0 (1)	1.45 (0.45,4.69)	0.886 ^b 0.538 ^c
	>18.6	6.5 (46)	10.9 (64)	0.0 (1)	1.29 (0.45,3.67)	0.633 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g1) Minimal (n=100)	≤18.6	0.15 (0.00,22.45)	0.660 ^b 0.454 ^c	AGE (p=0.044) ETHBACK (p=0.053)
	>18.6	0.48 (0.04,5.50)	0.553 ^c	SUN2HR (p<0.001)
h1) Maximal (n=230)	≤18.6	1.55 (0.40,6.01)	0.580 ^b 0.522 ^c	AGE (p=0.010) ETHBACK (p=0.057)
	>18.6	0.93 (0.28,3.12)	0.907 ^c	SUN2HR (p=0.009) SUNRPT (p=0.099) LAT (p=0.087) HAIR (p=0.115)

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Officer—Other Sites versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e2) Minimal (n=97)	≤18.6	3.3 (30)	0.0 (14)	-- (0)	--	--
	>18.6	4.0 (28)	4.0 (25)	-- (0)	0.58 (0.01,25.05)	0.777 ^c
f2) Maximal (n=226)	≤18.6	4.5 (66)	1.9 (53)	0.0 (1)	0.56 (0.08,4.12)	0.861 ^b 0.568 ^c
	>18.6	6.5 (46)	3.4 (59)	0.0 (1)	0.70 (0.15,3.31)	0.651 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g2) Minimal (n=97)	≤18.6	--	--	--
	>18.6	--	--	--
h2) Maximal (n=226)	≤18.6	0.52 (0.07,3.87)	0.811 ^b 0.527 ^c	SUNRPT (p=0.002)
	>18.6	0.71 (0.15,3.49)	0.677 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-12. (Continued)

Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Flyer—Ear, Face, Head, and Neck versus None)

Ranch Hands - Log ₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e3) Minimal (n=98)	≤18.6	12.5 (8)	8.8 (34)	20.0 (5)	0.98 (0.33,2.89)	0.972 ^c
	>18.6	12.5 (8)	0.0 (33)	0.0 (10)	--	--
f3) Maximal (n=122)	≤18.6	14.3 (14)	11.4 (35)	7.1 (14)	0.86 (0.41,1.82)	0.696 ^c
	>18.6	0.0 (7)	2.7 (37)	0.0 (15)	--	--

Ranch Hands - Log ₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g3) Minimal (n=94)	≤18.6	1.19 (0.39,3.63)	0.764 ^c	AGE (p=0.044) ETHBACK (p=0.053) SUN2HR (p<0.001)
	>18.6	--	--	
h3) Maximal (n=116)	≤18.6	0.62 (0.24,1.59)	0.318 ^c	AGE (p=0.010) ETHBACK (p=0.057) SUN2HR (p=0.009) SUNRPT (p=0.099) LAT (p=0.087) HAIR (p=0.115)
	>18.6	--	--	

^aRelative risk for a twofold increase in dioxin.

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Flyer—Other Sites versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e4) Minimal (n=98)	≤18.6	12.5 (8)	3.1 (32)	20.0 (5)	1.04 (0.26,4.18)	0.010 ^b 0.955 ^c
	>18.6	0.0 (7)	0.0 (33)	23.1 (13)	29.36 (1.22,705.1)	0.037 ^c
f4) Maximal (n=120)	≤18.6	0.0 (12)	6.1 (33)	7.1 (14)	1.48 (0.52,4.22)	0.017 ^b 0.459 ^c
	>18.6	0.0 (7)	0.0 (36)	16.7 (18)	29.37 (1.22,709.9)	0.038 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g4) Minimal (n=98)	≤18.6	1.18 (0.34,4.12)	0.017 ^b 0.794 ^c	SUNRPT (p<0.001)
	>18.6	37.63 (0.92, 1,545.8)	0.056 ^c	
h4) Maximal (n=120)	≤18.6	1.59 (0.60,4.22)	0.026 ^b 0.349 ^c	SUNRPT (p=0.002)
	>18.6	37.63 (0.92, 1,546.2)	0.056 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal-- Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal-- Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Groundcrew—Ear, Face, Head, and Neck versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e5) Minimal (n=272)	≤18.6	4.5 (22)	7.2 (69)	0.0 (47)	0.30 (0.09,1.01)	0.430 ^b 0.051 ^c
	>18.6	14.3 (14)	3.4 (59)	3.3 (61)	0.53 (0.24,1.16)	0.112 ^c
f5) Maximal (n=325)	≤18.6	5.3 (19)	7.5 (80)	0.0 (64)	0.53 (0.26,1.09)	0.314 ^b 0.086 ^c
	>18.6	0.0 (22)	6.6 (61)	2.5 (79)	0.84 (0.49,1.43)	0.523 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a		p-Value	Covariate Remarks	
g5) Minimal (n=266)	≤18.6	0.32 (0.09,1.08)		0.336 ^b 0.066 ^c	AGE (p=0.044) ETHBACK (p=0.053)	
	>18.6	0.63 (0.29,1.37)		0.242 ^c	SUN2HR (p<0.001)	
h5) Maximal (n=319)	≤18.6	0.54 (0.25,1.18)		0.221 ^b 0.123 ^c	AGE (p=0.010) ETHBACK (p=0.057)	
	>18.6	0.97 (0.55,1.70)		0.913 ^c	SUN2HR (p=0.009) SUNRPT (p=0.099) LAT (p=0.087) HAIR (p=0.115)	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal-- Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal-- Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Groundcrew—Other Sites versus None)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e6) Minimal (n=267)	≤18.6	4.5 (22)	4.5 (67)	2.1 (48)	0.61 (0.24,1.58)	0.986 ^b 0.313 ^c
	>18.6	0.0 (12)	3.4 (59)	0.0 (59)	0.61 (0.17,2.19)	0.444 ^c
f6) Maximal (n=319)	≤18.6	0.0 (18)	5.1 (78)	1.5 (65)	0.90 (0.44,1.82)	0.983 ^b 0.759 ^c
	>18.6	0.0 (22)	3.4 (59)	0.0 (77)	0.91 (0.37,2.22)	0.830 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g6) Minimal (n=267)	≤18.6	0.61 (0.23,1.58)	0.967 ^b 0.305 ^c	SUNRPT (p<0.001)
	>18.6	0.63 (0.18,2.15)	0.458 ^c	
h6) Maximal (n=319)	≤18.6	0.85 (0.42,1.74)	0.866 ^b 0.666 ^c	SUNRPT (p=0.002)
	>18.6	0.94 (0.39,2.26)	0.893 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal-- Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal-- Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Officer—Ear, Face, Head, and Neck versus None)
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	274	6.6	All Categories		0.723
Unknown	202	8.9	Unknown vs. Background	1.39 (0.70,2.75)	0.434
Low	37	5.4	Low vs. Background	0.81 (0.18,3.67)	0.999
High	2	0.0	High vs. Background	--	0.999
Total	515				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	267	All Categories		0.686	AGE (p=0.019) ETHBACK (p=0.020)
Unknown	199	Unknown vs. Background	1.32 (0.64,2.74)	0.449	SUN2HR (p=0.016)
Low	36	Low vs. Background	0.71 (0.15,3.45)	0.671	SUNRPT (p=0.049)
High	2	High vs. Background	--	--	LAT (p=0.020) HAIR (p=0.035)
Total	504				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Officer—Other Sites versus None)
(Verified)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	261	1.9	All Categories		0.555
Unknown	192	4.2	Unknown vs. Background	2.23 (0.72,6.93)	0.258
Low	36	2.8	Low vs. Background	1.46 (0.17,12.89)	0.999
High	2	0.0	High vs. Background	--	0.999
Total	491				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	260	All Categories		0.508	SUNRPT (p=0.010)
Unknown	192	Unknown vs. Background	2.34 (0.75,7.31)	0.144	
Low	36	Low vs. Background	1.51 (0.17,13.40)	0.709	
High	2	High vs. Background	--	--	
Total	490				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Flyer—Ear, Face, Head, and Neck versus None)
(Verified)**

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	114	7.0	All Categories		0.779
Unknown	39	7.7	Unknown vs. Background	1.10 (0.28,4.42)	0.999
Low	50	4.0	Low vs. Background	0.55 (0.11,2.72)	0.728
High	29	3.4	High vs. Background	0.47 (0.06,3.99)	0.842
Total	232				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	109	All Categories		0.668	AGE (p=0.019) ETHBACK (p=0.020)
Unknown	36	Unknown vs. Background	1.81 (0.41,8.10)	0.434	SUN2HR (p=0.016)
Low	49	Low vs. Background	0.75 (0.14,3.97)	0.735	SUNRPT (p=0.049)
High	28	High vs. Background	0.45 (0.05,4.12)	0.476	LAT (p=0.020) HAIR (p=0.035)
Total	222				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Flyer—Other Sites versus None)
(Verified)**

i4) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	108	1.9	All Categories		0.010
Unknown	36	0.0	Unknown vs. Background	--	0.999
Low	49	2.0	Low vs. Background	1.10 (0.10,12.47)	0.999
High	32	12.5	High vs. Background	7.57 (1.31,43.46)	0.049
Total	225				

j4) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	108	All Categories		0.055	SUNRPT (p=0.010)
Unknown	36	Unknown vs. Background	--	--	
Low	49	Low vs. Background	1.20 (0.10,13.75)	0.882	
High	32	High vs. Background	7.29 (1.23,42.71)	0.028	
Total	225				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Groundcrew—Ear, Face, Head, and Neck versus None)
(Verified)**

i5) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	338	3.8	All Categories		0.114
Unknown	84	4.8	Unknown vs. Background	1.25 (0.40,3.94)	0.896
Low	91	7.7	Low vs. Background	2.08 (0.81,5.39)	0.214
High	143	1.4	High vs. Background	0.36 (0.08,1.60)	0.256
Total	656				

j5) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	329	All Categories		0.149	AGE (p=0.019) ETHBACK (p=0.020)
Unknown	81	Unknown vs. Background	1.17 (0.36,3.85)	0.792	SUN2HR (p=0.016)
Low	89	Low vs. Background	2.17 (0.82,5.78)	0.119	SUNRPT (p=0.049)
High	140	High vs. Background	0.39 (0.09,1.80)	0.230	LAT (p=0.020) HAIR (p=0.035)
Total	639				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

TABLE 7-12. (Continued)

**Analysis of Sun Exposure-Related Malignant Skin Neoplasm by Occupation
(Enlisted Groundcrew—Other Sites versus None)
(Verified)**

i6) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	331	1.8	All Categories		0.091
Unknown	80	0.0	Unknown vs. Background	--	0.540
Low	88	4.5	Low vs. Background	2.58 (0.71,9.37)	0.274
High	142	0.7	High vs. Background	0.38 (0.05,3.23)	0.654
Total	641				

j6) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	331	All Categories		0.082	SUNRPT (p=0.010)
Unknown	80	Unknown vs. Background	--	--	
Low	88	Low vs. Background	2.47 (0.67,9.08)	0.171	
High	142	High vs. Background	0.37 (0.04,3.12)	0.360	
Total	641				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.

Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.

Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.

High (Ranch Hands): Current Dioxin >33.3 ppt.

without a sun exposure-related malignant skin neoplasm produced nonsignificant relative risks that were less than 1 (Table 7-12 [a3-d3]: $p > 0.10$ for all analyses).

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted flyers with a sun exposure-related malignant skin neoplasm on other sites versus Ranch Hand enlisted flyers without a sun exposure-related malignant skin neoplasm yielded a marginally significant relative risk greater than 2 (Table 7-12 [a4]: Est. RR=2.27, $p=0.052$). For this analysis, the relative frequencies of Ranch Hand enlisted flyers for low, medium, and high initial dioxin were 5.6, 1.7, and 18.2 percent. After adjusting for skin reaction to repeated sun exposure, the relative risk remained greater than 1 but became nonsignificant (Table 7-12 [c4]: $p=0.128$). Under the maximal assumption, the unadjusted relative risk for Ranch Hand enlisted flyers was significant with a relative risk greater than 2 (Table 7-12 [b4]: Est. RR=2.47, $p=0.015$) and associated relative frequencies of 0.0, 2.9, and 11.8 percent for low, medium, and high initial dioxin. Under the maximal assumption, the adjusted relative risk remained significant and greater than 2 (Table 7-12 [d4]: Adj. RR=2.14, $p=0.049$) after covariate adjustment.

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted groundcrew with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus Ranch Hand enlisted groundcrew without a sun exposure-related malignant skin neoplasm produced a relative risk that was significant but less than 1 (Table 7-12 [a5]: Est. RR=0.54, $p=0.022$). For this analysis, the relative frequencies of Ranch Hand enlisted groundcrew for low, medium, and high initial dioxin were 5.9, 6.0, and 1.9 percent. Under the maximal assumption, the unadjusted analysis produced a nonsignificant relative risk that also was less than 1 (Table 7-12 [b5]: $p=0.133$). After adjusting for age, ethnic background, and skin reaction after at least 2 hours of sun exposure, the relative risk under the minimal assumption became marginally significant (Table 7-12 [c5]: Adj. RR=0.56, $p=0.063$) but it was still less than 1. Under the maximal assumption, the adjusted relative risk remained nonsignificant (Table 7-12 [d5]: $p=0.265$).

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted groundcrew with a sun exposure-related malignant skin neoplasm for other sites versus Ranch Hand enlisted groundcrew without a sun exposure-related malignant skin neoplasm was marginally significant with a relative risk less than 1 (Table 7-12 [a6]: Est. RR=0.57, $p=0.098$) with relative frequencies for Ranch Hand enlisted groundcrew of 5.9, 3.1, and 1.0 for low, medium, and high initial dioxin. Under the maximal assumption, the unadjusted relative risk was nonsignificant (Table 7-12 [b6]: $p=0.507$). Under both assumptions, after adjusting for skin reaction to repeated sun exposure, the adjusted relative risks for Ranch Hand enlisted groundcrew were nonsignificant (Table 7-12 [c6] and [d6]: $p=0.104$ and $p=0.485$).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under both assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand officers with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus Ranch Hand officers without a sun exposure-related malignant skin neoplasm exhibited nonsignificant interactions between current dioxin and time since tour (Table 7-12 [e1-h1]: $p > 0.55$ for each interaction).

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand officers with a sun exposure-related malignant skin neoplasm for other sites versus Ranch Hand officers without a sun exposure-related malignant skin neoplasm displayed a nonsignificant risk for time over 18.6 years (Table 7-12 [e2]: $p=0.777$). The interaction and other time stratum were not evaluated for significance due to the sparse number of Ranch Hands with the neoplasms of interest in the later time stratum. Also, an adjusted analysis was not performed under the minimal assumption due to sparse data. Under the maximal assumption, the unadjusted and the adjusted analyses contained nonsignificant current dioxin-by-time interactions (Table 7-12 [f2] and [h2]: $p=0.861$ and $p=0.811$, respectively).

Under both assumptions, the unadjusted and the adjusted analyses of the frequency of Ranch Hand enlisted flyers with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus Ranch Hand enlisted flyers without a sun exposure-related malignant skin neoplasm were limited to the later time since tour stratum (18.6 years or less) because of the sparse number of Ranch Hands with the neoplasm of interest in the other time stratum. Under each assumption and for each analysis, the relative risks were nonsignificant (Table 7-12 [e3-h3]: $p>0.30$ for each analysis).

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted flyers with a sun exposure-related malignant skin neoplasm on other sites versus Ranch Hand enlisted flyers without a sun exposure-related malignant skin neoplasm contained a significant interaction between current dioxin and time (Table 7-12 [e4]: $p=0.010$). Ranch Hand enlisted flyers with the later tours (18.6 years or less) displayed a nonsignificant relative risk greater than 1 ($p=0.955$) and a significant relative risk greater than 1 for the other time stratum (Est. RR=29.36, $p=0.037$). The relative frequencies of Ranch Hand enlisted flyers for the earlier time stratum were 0.0, 0.0, and 23.1 percent for the low, medium, and high current dioxin categories.

Under the maximal assumption, the current dioxin-by-time interaction of the unadjusted analysis was also significant (Table 7-12 [f4]: $p=0.017$) with a nonsignificant relative risk greater than 1 for Ranch Hands with later tours ($p=0.459$) and a significant relative risk greater than 1 for Ranch Hands with earlier tours (Est. RR=29.37, $p=0.038$). The corresponding relative frequencies of Ranch Hand enlisted flyers within the earlier time stratum were 0.0, 0.0, and 16.7 percent. Significant interactions between current dioxin and time (Table 7-12 [g4] and [h4]: $p=0.017$ and $p=0.026$), and marginally significant relative risks (Adj. RR=37.63 and $p=0.056$ for minimal and maximal analyses) for the enlisted flyers with earlier tours also were found in the adjusted analyses. Ranch Hands with later tours exhibited nonsignificant relative risks (minimal assumption, $p=0.794$; maximal assumption, $p=0.349$).

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hand enlisted groundcrew with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus Ranch Hand enlisted groundcrew without a sun exposure-related malignant skin neoplasm contained a nonsignificant interaction between current dioxin and time (Table 7-12 [e5]: $p=0.430$). However, for time 18.6 years or less, the relative risk was marginally significant (Est. RR=0.30, $p=0.051$) but less than 1. The corresponding relative frequencies of Ranch Hand enlisted groundcrew within that time stratum were 4.5, 7.2, and 0.0 percent.

Under the maximal assumption, the unadjusted analysis also contained a nonsignificant interaction between current dioxin and time (Table 7-12 [f5]: $p=0.314$). Within the later time stratum, the relative risk was marginally significant but less than 1 (Est. RR=0.53, $p=0.086$) with relative frequencies of Ranch Hand enlisted groundcrew for that time stratum being 5.3, 7.5, and 0.0 percent. Under both assumptions, the adjusted analyses displayed nonsignificant interactions (Table 7-12 [g5] and [h5]: $p=0.336$ and $p=0.221$). Under the minimal assumption, however, the later time stratum contained a marginally significant relative risk that was less than 1 (Adj. RR=0.32, $p=0.066$).

Under each assumption, the unadjusted and the adjusted analyses of the frequency of Ranch Hand enlisted groundcrew with a sun exposure-related malignant skin neoplasm on other sites versus Ranch Hand enlisted groundcrew without a sun exposure-related malignant skin neoplasm contained nonsignificant interactions between current dioxin and time (Table 7-12 [e6]: $p>0.85$ for each interaction). The stratum-specific analyses were nonsignificant.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The frequencies of study participants with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus the frequencies of study participants without a sun exposure-related malignant skin neoplasm were compared for Ranch Hand officers in the unknown, low, and high current dioxin categories and for Comparison officers in the background category. The unadjusted and the adjusted analyses contained nonsignificant overall contrasts (Table 7-12 [i1] and [j1]: $p=0.723$ and $p=0.686$, respectively). Ranch Hand versus Comparison contrasts were nonsignificant.

The frequencies of study participants with a sun exposure-related malignant skin neoplasm on other sites versus the frequencies of study participants without a sun exposure-related malignant skin neoplasm were compared for Ranch Hand officers in the unknown, low, and high current dioxin categories and for Comparison officers in the background category. The unadjusted and the adjusted analyses displayed nonsignificant overall contrasts (Table 7-12 [i2] and [j2]: $p=0.555$ and $p=0.508$, respectively). Ranch Hand versus Comparison contrasts were nonsignificant.

The frequencies of study participants with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus the frequencies of study participants without a sun exposure-related malignant skin neoplasm were compared for Ranch Hand enlisted flyers in the unknown, low, and high current dioxin categories and for Comparison enlisted flyers in the background category. The unadjusted and the adjusted analyses exhibited nonsignificant overall contrasts (Table 7-12 [i3] and [j3]: $p=0.779$ and $p=0.668$, respectively). Ranch Hand versus Comparison contrasts were nonsignificant.

The frequencies of study participants with a sun exposure-related malignant skin neoplasm on other sites versus the frequencies of study participants without a sun exposure-related malignant skin neoplasm were compared for Ranch Hand enlisted flyers in the unknown, low, and high current dioxin categories and for Comparison enlisted flyers in the background category. The unadjusted analysis displayed a significant overall contrast (Table 7-12 [i4]: $p=0.010$). The relative frequencies of enlisted flyers with a sun exposure-related

malignant skin neoplasm on other sites for the background, unknown, low, and high current dioxin categories were 1.9, 0.0, 2.0, and 12.5 percent. The high versus background contrast was significant (Est. RR=7.57, 95% C.I.: [1.31,43.46], p=0.049). The unknown versus background and the low versus background contrasts were nonsignificant (p=0.999 for both contrasts). After adjusting for skin reaction after repeated sun exposure, the overall contrast was found to be marginally significant (Table 7-2 [j4]: p=0.055) with the high versus background contrast being significant (Adj. RR=7.29, 95% C.I.: [1.23,42.71], p=0.028) and the low versus background contrast being nonsignificant (p=0.882).

The frequencies of study participants with a sun exposure-related malignant skin neoplasm on the ear, face, head, and neck versus the frequencies of study participants without a sun exposure-related malignant skin neoplasm were compared for Ranch Hand enlisted groundcrew in the unknown, low, and high current dioxin categories and for Comparison enlisted groundcrew in the background category. The unadjusted and the adjusted analyses exhibited nonsignificant overall contrasts (Table 7-12 [i5] and [j5]: p=0.114 and p=0.149, respectively). The Ranch Hand versus Comparison contrasts were nonsignificant.

The frequencies of study participants with a sun exposure-related malignant skin neoplasm on other sites versus the frequencies of study participants without a sun exposure-related malignant skin neoplasm were compared for Ranch Hand enlisted groundcrew in the unknown, low, and high current dioxin categories and for Comparison enlisted groundcrew in the background category. The unadjusted analysis displayed a marginally significant overall contrast (Table 7-12 [i6]: p=0.091). The relative frequencies of participants within the background, unknown, low, and high current dioxin categories were 1.8, 0.0, 4.5, and 0.7 percent. None of the Ranch Hand versus Comparison contrasts was significant (p>0.25 for each contrast). The adjusted analysis also contained a marginally significant overall contrast (Table 7-12 [j6]: p=0.082) with nonsignificant Ranch Hand versus Comparison contrasts for low versus background (p=0.171) and high versus background (p=0.360).

Multiple Basal Cell Carcinoma

For the analyses focusing on multiple basal cell carcinomas, mutually exclusive categories were constructed consisting of participants with only one basal cell carcinoma, two or more basal cell carcinomas, and no basal cell carcinomas. Logistic regression models were then used to estimate and evaluate relative risks based only on the participants with one basal cell carcinoma versus no basal cell carcinomas and on those participants with two or more basal cell carcinomas versus none.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the unadjusted and the adjusted analyses of the frequency of Ranch Hands with one or no basal cell carcinomas, the relative risks were found to be nonsignificant and less than 1 using models with initial dioxin (Table 7-13 [a1-d1]: p>0.20 for each analysis).

In the unadjusted analysis of the frequency of Ranch Hands with multiple basal cell carcinomas versus no basal cell carcinomas, the relative risk was significant but less than 1 (Table 7-13 [a2]: Est. RR=0.49, p=0.026) under the minimal assumption. The relative frequencies of Ranch Hands with multiple basal cell carcinoma within the low, medium, and

TABLE 7-13.

**Analysis of Basal Cell Carcinoma
(One versus None)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a1) Minimal (n=478)	Low	113	7.1	0.82 (0.58,1.16)	0.244
	Medium	238	5.5		
	High	127	4.7		
b1) Maximal (n=689)	Low	178	6.7	0.89 (0.69,1.13)	0.314
	Medium	333	6.0		
	High	178	4.5		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c1) Minimal (n=466)	0.84 (0.59,1.20)		0.321	ETHBACK (p=0.107) SUN2HR (p=0.031) SUNRPT (p=0.064)	
d1) Maximal (n=673)	0.94 (0.73,1.21)		0.629	AGE (p=0.092) ETHBACK (p=0.067) SUN2HR (p=0.091) SUNRPT (p=0.084)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-13. (Continued)
Analysis of Basal Cell Carcinoma
(Multiple versus None)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a2) Minimal (n=462)	Low	110	4.5	0.49 (0.24,1.01)	0.026
	Medium	230	2.2		
	High	122	0.8		
b2) Maximal (n=664)	Low	169	1.8	0.74 (0.48,1.14)	0.147
	Medium	324	3.4		
	High	171	0.6		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c2) Minimal (n=462)	0.59 (0.28,1.26)		0.127	AGE (p=0.084) HAIR (p=0.062)	
d2) Maximal (n=664)	0.80 (0.49,1.28)		0.324	AGE (p=0.032) SUNRPT (p=0.117) HAIR (p=0.070)	

^aRelative risk for a twofold increase in dioxin.
 Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-13. (Continued)
Analysis of Basal Cell Carcinoma
(One versus None)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e1) Minimal (n=478)	≤18.6	7.8 (64)	6.0 (117)	5.6 (54)	0.77 (0.45,1.33)	0.926 ^b 0.347 ^c
	>18.6	7.8 (51)	4.2 (119)	4.1 (73)		0.80 (0.48,1.33)
f1) Maximal (n=689)	≤18.6	6.1 (99)	8.0 (174)	3.7 (81)	0.90 (0.63,1.28)	0.874 ^b 0.544 ^c
	>18.6	6.4 (78)	5.6 (160)	3.1 (97)		0.86 (0.60,1.24)

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g1) Minimal (n=466)			0.967 ^b	ETHBACK (p=0.111)
	≤18.6	0.80 (0.47,1.37)	0.418 ^c	SUN2HR (p=0.033)
	>18.6	0.82 (0.49,1.35)	0.428 ^c	SUNRPT (p=0.063)
h1) Maximal (n=673)			0.776 ^b	AGE (p=0.074)
	≤18.6	0.99 (0.68,1.43)	0.949 ^c	ETHBACK (p=0.064)
	>18.6	0.92 (0.63,1.34)	0.652 ^c	SUN2HR (p=0.098) SUNRPT (p=0.081)

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-13. (Continued)
Analysis of Basal Cell Carcinoma
(Multiple versus None)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)^a	p-Value
		Low	Medium	High		
e2) Minimal (n=462)	≤18.6	1.7 (60)	3.5 (114)	0.0 (51)	0.50 (0.16,1.60)	0.866 ^b 0.247 ^c
	>18.6	6.0 (50)	1.7 (116)	1.4 (71)	0.44 (0.16,1.24)	0.121 ^c
f2) Maximal (n=664)	≤18.6	3.1 (96)	3.0 (165)	0.0 (78)	0.69 (0.35,1.36)	0.731 ^b 0.282 ^c
	>18.6	0.0 (73)	3.8 (157)	1.1 (95)	0.81 (0.45,1.45)	0.471 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
g2) Minimal (n=462)	≤18.6	0.66 (0.20,2.22)		0.911 ^b 0.506 ^c	AGE (p=0.100) HAIR (p=0.062)	
	>18.6	0.61 (0.22,1.65)		0.327 ^c		
h2) Maximal (n=664)	≤18.6	0.79 (0.37,1.68)		0.772 ^b 0.546 ^c	AGE (p=0.029) SUNRPT (p=0.117)	
	>18.6	0.92 (0.49,1.73)		0.788 ^c	HAIR (p=0.067)	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-13. (Continued)

**Analysis of Basal Cell Carcinoma
(One versus None)
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	732	5.7	All Categories		0.524
Unknown	324	6.5	Unknown vs. Background	1.14 (0.66,1.96)	0.732
Low	179	6.1	Low vs. Background	1.08 (0.54,2.13)	0.950
High	178	3.4	High vs. Background	0.57 (0.24,1.37)	0.276
Total	1,413				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	712	All Categories		0.515	ETHBACK (p=0.097) SUN2HR (p=0.035)
Unknown	315	Unknown vs. Background	1.13 (0.64,1.98)	0.672	SUNRPT (p=0.027)
Low	175	Low vs. Background	1.18 (0.59,2.36)	0.646	LAT (p=0.120)
High	174	High vs. Background	0.60 (0.25,1.44)	0.250	XRAY (p=0.042)
Total	1,376				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-13. (Continued)

**Analysis of Basal Cell Carcinoma
(Multiple versus None)
(Verified)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	697	1.0	All Categories		0.053
Unknown	312	2.9	Unknown vs. Background	2.93 (1.08,7.93)	0.060
Low	173	2.9	Low vs. Background	2.93 (0.92,9.36)	0.139
High	173	0.6	High vs. Background	0.57 (0.07,4.69)	0.999
Total	1,355				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	691	All Categories		0.078	AGE (p=0.012) SUN2HR (p=0.048)
Unknown	311	Unknown vs. Background	2.95 (1.05,8.29)	0.039	SUNRPT (p=0.038)
Low	173	Low vs. Background	3.59 (1.07,12.04)	0.038	LAT (p=0.026)
High	173	High vs. Background	0.89 (0.11,7.56)	0.915	HAIR (p<0.001)
Total	1,348				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

high initial dioxin categories were 4.5, 2.2, and 0.8 percent. Under the maximal assumption, the unadjusted relative risk was nonsignificant (Table 7-13 [b2]: $p=0.147$). After adjusting for age and hair color in the minimal analysis, the adjusted relative risk became nonsignificant (Table 7-13 [c2]: $p=0.127$). In the maximal analysis, the adjusted relative risk remained nonsignificant (Table 7-13 [d2]: $p=0.324$).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

In the unadjusted and the adjusted analyses of the frequency of Ranch Hands with one or no basal cell carcinomas, the interactions between current dioxin and time since tour were nonsignificant under both the minimal and maximal assumption (Table 7-13 [e1-h1]: $p>0.75$ for each interaction). Corresponding unadjusted and adjusted analyses of the frequency of Ranch Hands with multiple basal cell carcinomas versus no basal cell carcinomas also found nonsignificant current dioxin-by-time interactions (Table 7-13 [e2-h2]: $p>0.70$ for each interaction). All relative risks within each time stratum were less than 1 and nonsignificant.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted and the adjusted analyses of the frequency of participants with one basal cell carcinoma versus no basal cell carcinomas, the overall contrasts of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background current dioxin category were nonsignificant (Table 7-13 [i1] and [j1]: $p=0.524$ and $p=0.515$, respectively). All Ranch Hand versus Comparison contrasts were nonsignificant.

In the unadjusted analysis of the frequency of participants with multiple basal cell carcinomas versus no basal cell carcinomas, the overall contrast was marginally significant (Table 7-13 [i2]: $p=0.053$). The relative frequencies of participants with multiple basal cell carcinomas were 1.0, 2.9, 2.9, and 0.6 percent for the background, unknown, low, and high current dioxin categories. The unknown versus background contrast was marginally significant with a relative risk greater than 1 (Est. RR=2.93, 95% C.I.: [1.08,7.93], $p=0.060$). The low versus background contrast was nonsignificant ($p=0.139$) as was the high versus background contrast ($p=0.999$). After adjusting for age, average lifetime residential latitude, hair color, and the two skin reaction to sun exposure covariates, the overall contrast remained marginally significant (Table 7-13 [j2]: $p=0.078$). The unknown versus background contrast became significant (Adj. RR=2.95, 95% C.I.: [1.05,8.29], $p=0.039$) as did the low versus background contrast (Adj. RR=3.59, 95% C.I.: [1.07,12.04], $p=0.038$). The high versus background contrast remained nonsignificant ($p=0.915$) in the adjusted analysis.

All Systemic Neoplasms

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified systemic neoplasm (malignant plus benign) exhibited a nonsignificant relative risk greater than 1 with respect to initial dioxin (Table 7-14 [a]: $p=0.319$). Under the maximal assumption, the unadjusted analysis revealed a significant relative risk greater than 1 (Table 7-14 [b]: Est. RR=1.28, $p=0.009$). The relative frequencies of Ranch Hands with a verified systemic neoplasm under the maximal assumption were 2.2, 9.7, and 10.2 percent for the low, medium, and high initial dioxin category. Under the minimal assumption, the relative risk remained nonsignificant after covariate adjustment (Table 7-14 [c]: $p=0.109$). Under the

TABLE 7-14.

Analysis of All Systemic Neoplasms

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a) Minimal (n=521)	Low	130	7.7	1.13 (0.89,1.42)	0.319
	Medium	260	8.8		
	High	131	13.0		
b) Maximal (n=742)	Low	185	2.2	1.28 (1.07,1.53)	0.009
	Medium	371	9.7		
	High	186	10.2		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c) Minimal (n=515)	1.22 (0.96,1.55)		0.109	AGE (p=0.005) RACE (p=0.147) CARCIN (p=0.121)	
d) Maximal (n=722)	1.32 (1.09,1.61)		0.006	AGE (p=0.002) RACE (p=0.118) CARCIN (p=0.041) DRKYR (p=0.082)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-14. (Continued)
Analysis of All Systemic Neoplasms

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	11.1 (72)	7.0 (128)	9.3 (54)	0.97 (0.64,1.47)	0.445 ^b 0.868 ^c
	>18.6	5.2 (58)	10.6 (132)	14.3 (77)	1.18 (0.88,1.58)	0.277 ^c
f) Maximal (n=742)	≤18.6	2.8 (106)	8.4 (191)	7.2 (83)	1.26 (0.93,1.70)	0.860 ^b 0.139 ^c
	>18.6	6.3 (79)	8.4 (179)	13.5 (104)	1.22 (0.96,1.53)	0.098 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a		p-Value	Covariate Remarks	
g) Minimal (n=515)	≤18.6	1.14 (0.74,1.76)		0.635 ^b 0.565 ^c	AGE (p=0.006) CARCIN (p=0.133)	
	>18.6	1.29 (0.95,1.75)		0.105 ^c		
h) Maximal (n=722)	≤18.6	1.42 (1.02,1.98)		0.564 ^b 0.036 ^c	AGE (p=0.001) RACE (p=0.116) DRKYR (p=0.073) CARCIN (p=0.038)	
	>18.6	1.26 (0.99,1.62)		0.065 ^c		

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-14. (Continued)
Analysis of All Systemic Neoplasms
(Verified)

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	8.3	All Categories		0.087
Unknown	345	5.2	Unknown vs. Background	0.61 (0.36,1.05)	0.072
Low	196	9.7	Low vs. Background	1.19 (0.70,2.04)	0.524
High	187	10.7	High vs. Background	1.33 (0.78,2.25)	0.294
Total	1,514				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.021	AGE (p<0.001)
Unknown	345	Unknown vs. Background	0.59 (0.35,1.02)	0.057	
Low	196	Low vs. Background	1.21 (0.70,2.08)	0.488	
High	187	High vs. Background	1.65 (0.96,2.83)	0.072	
Total	1,514				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-14. (Continued)

**Analysis of All Systemic Neoplasms
(Verified and Suspected)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	8.4	All Categories		0.084
Unknown	345	5.2	Unknown vs. Background	0.60 (0.35,1.03)	0.063
Low	196	9.7	Low vs. Background	1.17 (0.69,2.00)	0.564
High	187	10.7	High vs. Background	1.31 (0.77,2.22)	0.321
Total	1,514				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.022	AGE (p<0.001)
Unknown	345	Unknown vs. Background	0.58 (0.34,1.00)	0.050	
Low	196	Low vs. Background	1.19 (0.69,2.04)	0.528	
High	187	High vs. Background	1.61 (0.94,2.77)	0.085	
Total	1,514				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

maximal assumption, the relative risk remained significant and greater than 1 in the adjusted analysis (Table 7-14 [d]: Adj. RR=1.32, p=0.006).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

In the unadjusted minimal and maximal analyses of the frequency of Ranch Hands with a verified systemic neoplasm, the interactions between current dioxin and time since tour were nonsignificant (Table 7-14 [e] and [f]: p=0.445 and p=0.860, respectively). Under the maximal assumption, Ranch Hands whose time since tour exceeded 18.6 years displayed a marginally significant relative risk greater than 1 (Est. RR=1.22, p=0.098). For that time stratum, the relative frequencies of Ranch Hands with low, medium, and high current dioxin were 6.3, 8.4, and 13.5 percent. Under the minimal and maximal assumptions, the interactions between current dioxin and time in the adjusted analyses were nonsignificant (Table 7-14 [g] and [h]: p=0.635 and p=0.564, respectively); thus the relative risks of the two time strata were not significantly different. However, under the maximal assumption, Ranch Hands with later tours displayed a significant adjusted relative risk greater than 1 (Adj. RR=1.42, p=0.036) and Ranch Hands with earlier tours displayed a marginally significant adjusted relative risk greater than 1 (Adj. RR=1.26, p=0.065) also.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the relative frequency of participants with a verified systemic neoplasm, the overall contrast of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background current dioxin category was marginally significant (Table 7-14 [i1]: p=0.087). The relative frequencies of participants with a verified systemic neoplasm for the background, unknown, low, and high current dioxin categories were 8.3, 5.2, 9.7, and 10.7 percent. The unknown versus background contrast was also marginally significant (p=0.072) with a relative risk less than 1 (Est. RR=0.61, 95% C.I.: [0.36,1.05]). The low versus background and the high versus background contrasts were nonsignificant (p=0.524 and p=0.294, respectively). After adjusting for age, the overall contrast became significant (Table 7-14 [j1]: p=0.021). The unknown versus background contrast displayed a marginally significant adjusted relative risk that was less than 1 (Adj. RR=0.59, 95% C.I.: [0.35,1.02], p=0.057); the high versus background contrast exhibited a marginally significant relative risk greater than 1 (Adj. RR=1.65, 95% C.I.: [0.96,2.83], p=0.072); and the low versus background contrast was nonsignificant (p=0.488).

The corresponding unadjusted analysis of the combination of verified and suspected systemic neoplasms was also marginally significant (Table 7-14 [i2]: p=0.084) with relative frequencies of 8.4, 5.2, 9.7, and 10.7 percent for the background, unknown, low, and high current dioxin categories. The unknown versus background contrast was also marginally significant with a relative risk less than 1 (Est. RR=0.60, 95% C.I.: [0.35,1.03], p=0.063). The other two Ranch Hand contrasts were nonsignificant (p>0.30). Adjusting for age, the overall contrast was significant (Table 7-14 [j2]: p=0.022). The unknown versus background contrast was significant with an adjusted relative risk less than 1 (Adj. RR=0.58, 95% C.I.: [0.34,1.00], p=0.050) and the high versus background contrast was marginally significant with an adjusted relative risk greater than 1 (Adj. RR=1.61, 95% C.I.: [0.94, 2.77], p=0.085). The low versus background contrast had an adjusted relative risk that was greater than 1 but nonsignificant (p=0.528).

Malignant Systemic Neoplasms

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal assumption, the unadjusted analysis of the frequency of Ranch Hands with a verified malignant systemic neoplasm exhibited a significant relative risk with respect to initial dioxin (Table 7-15 [a]: Est. RR=0.56, p=0.048). However, the relative risk was less than 1. For that analysis, the relative frequencies of Ranch Hands with a verified malignant systemic neoplasm within the low, medium, and high initial dioxin categories were 1.5, 3.8, and 0.0 percent. Under the maximal assumption, the unadjusted analysis revealed a nonsignificant relative risk that also was less than 1 (Table 7-15 [b]: p=0.598). Under each assumption, the adjusted relative risk was nonsignificant (Table 7-15 [c] and [d]: p=0.144 and p=0.859).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under both assumptions, the unadjusted analyses of the frequency of Ranch Hands with a verified malignant systemic neoplasm displayed nonsignificant interactions between current dioxin and time since tour (Table 7-15 [e] and [f]: p=0.908 and p=0.352). The corresponding adjusted analyses also displayed nonsignificant interactions between current dioxin and time since tour (Table 7-15 [g] and [h]: p=0.899 and p=0.317). Associations with current dioxin were not significant within each time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the relative frequency of participants with a verified malignant systemic neoplasm, the overall contrast of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background current dioxin category was significant (Table 7-15 [i]: p=0.001). The relative frequencies of participants with a verified malignant systemic neoplasm for the background, unknown, low, and high categories were 1.7, 1.2, 5.1, and 0.0 percent. The low versus background contrast was also significant with a relative risk greater than 1 (Est. RR=3.20, 95% C.I.: [1.38,7.40], p=0.016). The other two Ranch Hand versus Comparison contrasts were nonsignificant (p=0.740 and p=0.122 for the unknown versus background and high versus background contrasts). The adjusted analysis for verified malignant systemic neoplasms also contained a significant overall contrast (Table 7-15 [j]: p=0.002) with a nonsignificant unknown versus background contrast (p=0.502) and a significant low versus background contrast (Adj. RR=3.51, 95% C.I.: [1.50,8.25], p=0.004).

Benign Systemic Neoplasms

Among the 42 Ranch Hands with nonmalignant systemic cancer, 45 different benign systemic neoplasms were identified. Lipomas accounted for 75.6 percent (34/45) of the total; 91.2 percent (31/34) of the lipomas were found in the subcutaneous tissues at various body locations. Three hemangiomas, two dermoid cysts, two fibromas, one benign adenolymphoma, one neurofibroma, one facial fibroma, and one adenoma were also found.

Among the 47 Comparisons with benign systemic cancer, 47 different systemic neoplasms were identified. Lipomas accounted for 70.2 percent (33/47). Of these, 90.9 percent (30/33) were in the subcutaneous tissue of various body locations. Also identified were five benign neoplasms where the cell type was not specified (one each in maxillary

TABLE 7-15.

Analysis of Malignant Systemic Neoplasms

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a) Minimal (n=521)	Low	130	1.5	0.56 (0.29,1.07)	0.048
	Medium	260	3.8		
	High	131	0.0		
b) Maximal (n=742)	Low	185	0.5	0.90 (0.60,1.35)	0.598
	Medium	371	3.5		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c) Minimal (n=521)	0.63 (0.32,1.25)		0.144	AGE (p=0.019)	
d) Maximal (n=733)	0.96 (0.63,1.48)		0.859	AGE (p=0.027) DRKYR (p=0.135)	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-15. (Continued)
Analysis of Malignant Systemic Neoplasms

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	<u>Percent Yes/(n) Current Dioxin</u>			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	2.8 (72)	3.1 (128)	0.0 (54)	0.53 (0.19,1.52)	0.908 ^b 0.238 ^c
	>18.6	0.0 (58)	4.5 (132)	0.0 (77)	0.49 (0.18,1.31)	0.154 ^c
f) Maximal (n=742)	≤18.6	0.0 (106)	3.1 (191)	0.0 (83)	1.06 (0.56,2.00)	0.352 ^b 0.858 ^c
	>18.6	2.5 (79)	3.4 (179)	0.0 (104)	0.70 (0.38,1.28)	0.247 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	0.66 (0.22,1.94)	0.899 ^b 0.448 ^c	AGE (p=0.026)
	>18.6	0.60 (0.23,1.59)	0.302 ^c	
h) Maximal (n=742)	≤18.6	1.24 (0.63,2.44)	0.317 ^b 0.525 ^c	AGE (p=0.014)
	>18.6	0.78 (0.41,1.47)	0.440 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-15. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Verified)**

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	1.7	All Categories		0.001
Unknown	345	1.2	Unknown vs. Background	0.70 (0.23,2.16)	0.740
Low	196	5.1	Low vs. Background	3.20 (1.38,7.40)	0.016
High	187	0.0	High vs. Background	--	0.122
Total	1,514				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.002	AGE (p=0.003) DRKYR (p=0.128)
Unknown	342	Unknown vs. Background	0.68 (0.22,2.11)	0.502	
Low	194	Low vs. Background	3.51 (1.50,8.25)	0.004	
High	183	High vs. Background	--	--	
Total	1,503				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.

Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.

Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.

High (Ranch Hands): Current Dioxin >33.3 ppt.

sinus, connective tissue of the breast, spermatic cord, urinary bladder, and thyroid gland), two hemangiomas, two papillomas, one benign mesothelioma, one fibroma, one neurilemmoma, one intradermal nevus, and one adenomatous polyp.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal and maximal assumptions, the unadjusted analysis of the frequency of Ranch Hands with a verified benign systemic neoplasm exhibited a significant relative risk that was greater than 1 (Table 7-16 [a] and [b]: Est. RR=1.36, p=0.022 and Est. RR=1.41, p=0.001, respectively). In the minimal analysis, the relative frequencies of Ranch Hands with a verified benign systemic neoplasm for the low, medium, and high initial dioxin categories were 5.4, 4.6, and 12.2 percent. In the maximal analysis, the corresponding relative frequencies were 1.6, 5.7, and 9.7 percent. The adjusted analyses also produced significant relative risks that were greater than 1 under both assumptions (Table 7-16 [c] and [d]: Adj. RR=1.40, p=0.015 and Adj. RR=1.49, p<0.001).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal and maximal assumptions, the unadjusted analysis for verified benign systemic neoplasms displayed nonsignificant current dioxin-by-time since tour interactions (Table 7-16 [e] and [f]: p=0.583 and p=0.879, respectively). For both assumptions, Ranch Hands with earlier tours (i.e., over 18.6 years) had significant relative risks that exceeded 1 (minimal assumption, Est. RR=1.42, p=0.035; maximal assumption, Est. RR=1.39, p=0.013). In the minimal analysis, the relative frequencies of participants with a verified benign systemic neoplasm for low, medium, and high current dioxin were 3.4, 6.1, and 13.0 percent for the earlier tour stratum. In the maximal analysis, the corresponding relative frequencies were 3.8, 4.5, and 12.5 percent for the same time stratum. Under the maximal assumption, the relative risk for Ranch Hands with later tours (i.e., ≤18.6 years) also displayed a marginally significant relative risk greater than 1 (Est. RR=1.35, p=0.095). The associated relative frequencies were 2.8, 4.7, and 7.2 percent for low, medium, and high current dioxin.

Under the minimal assumption, an adjusted model produced a nonsignificant interaction between current dioxin and time (Table 7-16 [g]: p=0.610) and a significant relative risk (Adj. RR=1.45, p=0.026) greater than 1 for Ranch Hands with earlier tours (over 18.6 years). Under the maximal assumption, an adjusted model containing the covariates of age and race also displayed a nonsignificant interaction between current dioxin and time (Table 7-16 [h]: p=0.964); although there were significant relative risks greater than 1 for each time stratum (≤18.6 years: Adj. RR=1.50, p=0.030; >18.6 years: Adj. RR=1.52, p=0.003).

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis, the overall contrast of the relative frequencies of participants with a verified benign systemic neoplasm for Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background current dioxin category was significant (Table 7-16 [i]: p=0.044). The relative frequencies of participants with a verified benign systemic neoplasm within the background, unknown, low, and high current dioxin categories were 6.0, 4.1, 4.6, and 10.2 percent. Of the three Ranch Hand versus Comparison contrasts, only the high versus background contrast was significant with a relative risk greater than 1 (Est. RR=1.78, 95% C.I.: [1.02,3.11], p=0.043). The other two contrasts had relative risks less than 1 and were nonsignificant (p>0.15).

TABLE 7-16.
Analysis of Benign Systemic Neoplasms

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.) ^a	p-Value
a) Minimal (n=521)	Low	130	5.4	1.36 (1.05,1.76)	0.022
	Medium	260	4.6		
	High	131	12.2		
b) Maximal (n=742)	Low	185	1.6	1.41 (1.15,1.72)	0.001
	Medium	371	5.7		
	High	186	9.7		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c) Minimal (n=521)	1.40 (1.07,1.81)	0.015	RACE (p=0.136)
d) Maximal (n=731)	1.49 (1.20,1.84)	<0.001	AGE (p=0.019) RACE (p=0.135) CARCIN (p=0.133)

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-16. (Continued)
Analysis of Benign Systemic Neoplasms

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	6.9 (72)	3.9 (128)	9.3 (54)	1.21 (0.76,1.93)	0.583 ^b 0.414 ^c
	>18.6	3.4 (58)	6.1 (132)	13.0 (77)	1.42 (1.03,1.96)	0.035 ^c
f) Maximal (n=742)	≤18.6	2.8 (106)	4.7 (191)	7.2 (83)	1.35 (0.95,1.91)	0.879 ^b 0.095 ^c
	>18.6	3.8 (79)	4.5 (179)	12.5 (104)	1.39 (1.07,1.81)	0.013 ^c

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	1.26 (0.79,2.00)	0.610 ^b 0.340 ^c	RACE (p=0.148)
	>18.6	1.45 (1.04,2.02)	0.026 ^c	
h) Maximal (n=742)	≤18.6	1.50 (1.04,2.17)	0.964 ^b 0.030 ^c	AGE (p=0.016) RACE (p=0.125)
	>18.6	1.52 (1.15,2.00)	0.003 ^c	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-16. (Continued)
Analysis of Benign Systemic Neoplasms
(Verified)

i) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	6.0	All Categories		0.044
Unknown	345	4.1	Unknown vs. Background	0.67 (0.36,1.23)	0.190
Low	196	4.6	Low vs. Background	0.76 (0.36,1.57)	0.455
High	187	10.2	High vs. Background	1.78 (1.02,3.11)	0.043
Total	1,514				

j) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.011	AGE (p=0.001)
Unknown	345	Unknown vs. Background	0.65 (0.35,1.20)	0.165	
Low	196	Low vs. Background	0.76 (0.37,1.59)	0.472	
High	187	High vs. Background	2.13 (1.20,3.79)	0.010	
Total	1,514				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

In the adjusted analysis of the frequency of participants with a verified benign systemic neoplasm, the overall contrast was also significant ($p=0.011$) as was the high versus background contrast (Adj. RR=2.13, 95% C.I.: [1.20,3.79], $p=0.010$). The other two Ranch Hand versus Comparison relative risks were nonsignificant and less than 1 ($p>0.15$ for both contrasts).

Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal and the maximal assumptions, the unadjusted analysis of the frequency of Ranch Hands with a verified systemic neoplasm of uncertain behavior or unspecified nature was nonsignificant with respect to initial dioxin (Table 7-17 [a] and [b]: $p=0.693$ and $p=0.691$, respectively). Both analyses were based on three Ranch Hands with a systemic neoplasm of uncertain behavior or unspecified nature. Because of the sparse number of Ranch Hands with these neoplasms, the adjusted analyses considered only the age covariate. The adjusted relative risk under each assumption was nonsignificant (Table 7-17 [c] and [d]: $p=0.947$ and $p=0.498$).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under each assumption, three Ranch Hands had a verified systemic neoplasm of uncertain behavior or unspecified nature (one Ranch Hand within time less than or equal to 18.6 years and two Ranch Hands within time over 18.6 years). Due to the sparse number of Ranch Hands with these neoplasms, the interaction and relative risk for the later time since tour stratum were not evaluated for significance under either assumption. Under the minimal and maximal assumptions, the relative risks for time over 18.6 years were nonsignificant (Table 7-17 [e] and [f]: $p=0.865$ and $p=0.696$, respectively). Because of the sparse numbers of Ranch Hands with these neoplasms, adjusted analyses were not performed.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The overall contrast of the relative frequencies of Ranch Hands and Comparisons with a verified systemic neoplasm of uncertain behavior or unspecified nature was nonsignificant (Table 7-17 [i1]: $p=0.253$). In this analysis, six Comparisons and one Ranch Hand had a verified systemic neoplasm. In the adjusted analysis, age was not retained in the final model; hence, the unadjusted and the adjusted results were the same. The overall contrast was also nonsignificant after including one suspected neoplasm (from a Comparison) with the preceding verified neoplasms (Table 7-17 [i2]: $p=0.184$). No covariates were retained in the final adjusted model; therefore, the unadjusted and the adjusted results were identical.

Systemic Neoplasms by Location/Site

The specified locations/sites used in the analyses of systemic neoplasms were determined from the locations/sites that were presented in the preceding AFHS report on the 1987 examination study (80). In many of these analyses, the number of participants with a systemic neoplasm for a specified location/site was very small or zero, thereby precluding an unadjusted and/or adjusted analysis. For completeness of documentation on analyses affected by sparse data, the relative frequencies and sample sizes are provided without the associated relative risks, confidence intervals, and p-values. Because of sparse numbers,

TABLE 7-17.

Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a) Minimal (n=521)	Low	130	0.8	0.82 (0.28,2.34)	0.693
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=742)	Low	185	0.0	1.17 (0.55,2.52)	0.691
	Medium	371	0.5		
	High	186	0.5		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c) Minimal (n=521)	0.97 (0.33,2.81)		0.947	AGE (p=0.124)	
d) Maximal (n=742)	1.33 (0.61,2.93)		0.498	AGE (p=0.110)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-17. (Continued)

Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	1.4 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	1.7 (58)	0.0 (132)	1.3 (77)	0.90 (0.28,2.90)	0.865 ^b
f) Maximal (n=742)	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.6 (179)	1.0 (104)	1.19 (0.49,2.91)	0.696 ^b

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-17. (Continued)

**Analysis of Systemic Neoplasms of Uncertain
Behavior or Unspecified Nature
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.8	All Categories		0.253
Unknown	345	0.0	Unknown vs. Background	--	0.224
Low	196	0.0	Low vs. Background	--	0.524
High	187	0.5	High vs. Background	0.70 (0.08,5.84)	0.999
Total	1,514				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.253	--
Unknown	345	Unknown vs. Background	--	0.224	
Low	196	Low vs. Background	--	0.524	
High	187	High vs. Background	0.70 (0.08,5.84)	0.999	
Total	1,514				

--: Relative risk and confidence interval not given due to the sparse number of abnormalities.
 Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-17. (Continued)

**Analysis of Systemic Neoplasms of Uncertain
Behavior or Unspecified Nature
(Verified and Suspected)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.9	All Categories		0.184
Unknown	345	0.0	Unknown vs. Background	--	0.155
Low	196	0.0	Low vs. Background	--	0.418
High	187	0.5	High vs. Background	0.60 (0.07,4.89)	0.999
Total	1,514				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.184	--
Unknown	345	Unknown vs. Background	--	0.155	
Low	196	Low vs. Background	--	0.418	
High	187	High vs. Background	0.60 (0.07,4.89)	0.999	
Total	1,514				

--: Relative risk and confidence interval not given due to the sparse number of abnormalities.
 Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

age was the only covariate used as a candidate covariate for any adjusted analysis that was undertaken in this section.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

Under the minimal and maximal assumptions, no Ranch Hands had a verified malignant systemic neoplasm for the ear, face, head, and neck (Table 7-18 [a1-d1]); oral cavity, pharynx, and larynx (Table 7-18 [a2-d2]); brain (Table 7-18 [a3-d3]); thymus and mediastinum (Table 7-18 [a4-d4]); thyroid gland (Table 7-18 [a5-d5]); colon and rectum (Table 7-18 [a7-d7]); ill-defined sites (Table 7-18 [a11-d11]); carcinoma in situ of penis (Table 7-18 [a12-d12]); and Hodgkin's disease (Table 7-18 [a14-d14]).

Under the minimal and maximal assumptions, only one Ranch Hand had a verified malignant systemic neoplasm of the bronchus and lung (Table 7-18 [a6-d6]); carcinoma in situ of other and unspecified sites (Table 7-18 [a13-d13]), and leukemia (Table 7-18 [a15-d15]).

Under the minimal assumption, four Ranch Hands had a verified malignant systemic neoplasm of the kidney and bladder. The relative risk was nonsignificant in the unadjusted analysis using initial dioxin (Table 7-18 [a8]: $p=0.368$). Under the maximal assumption, five Ranch Hands had a verified malignant systemic neoplasm of the kidney and bladder. Again, the relative risk was nonsignificant (Table 7-18 [b8]: $p=0.673$). An adjusted analysis under the minimal assumption was performed adjusting only for the covariate of age; the relative risk was not significant (Table 7-18 [c8]): $p=0.583$). Age was not retained in the maximal adjusted analyses; therefore, the unadjusted and adjusted results were identical (Table 7-18 [b8] and [d8]).

Under the minimal and maximal assumptions, two Ranch Hands had a verified malignant systemic neoplasm of the prostate. In the unadjusted analyses, neither relative risk was significant (Table 7-18 [a9] and [b9]: $p=0.522$ and $p=0.933$). Adjusted analyses were not performed because of the sparse data.

Under the minimal and maximal assumptions, three Ranch Hands had a verified malignant systemic neoplasm of the testicles. In the unadjusted analyses, neither relative risk was significant (Table 7-18 [a10] and [b10]: $p=0.363$ and $p=0.999$). Due to the sparse frequency of Ranch Hands with these neoplasms, adjusted analyses were performed using only age as a candidate covariate. Under both assumptions, age was not retained in the model, hence the unadjusted and adjusted analyses were identical.

Under the minimal assumption, only one Ranch Hand had a verified malignant systemic neoplasm of lymphoid and histiocytic tissue (Table 7-18 [a16]). Under the maximal assumption, two Ranch Hands had verified malignant systemic neoplasms of lymphoid and histiocytic tissue. In the maximal analysis, the relative risk was nonsignificant (Table 7-18 [b16]: $p=0.745$). No adjusted analyses were performed due to the sparse number of Ranch Hands with these neoplasms.

TABLE 7-18.

**Analysis of Malignant Systemic Neoplasms
(Ear, Face, Head, and Neck)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a1) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b1) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c1) Minimal (n=521)	--		--	--	
d1) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Oral Cavity, Pharynx, and Larynx)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a2) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b2) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c2) Minimal (n=521)	--		--	--	
d2) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Brain)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a3) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b3) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption			Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
c3) Minimal (n=521)			--	--	--
d3) Maximal (n=742)			--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Thymus and Mediastinum)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a4) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b4) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		

Ranch Hands - Log₂ (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c4) Minimal (n=521)	--	--	--
d4) Maximal (n=742)	--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Thyroid Gland)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a5) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b5) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption			Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c5) Minimal (n=521)			--	--	--
d5) Maximal (n=742)			--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Bronchus and Lung)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a6) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.4		
	High	131	0.0		
b6) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.3		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c6) Minimal (n=521)	--		--	--	
d6) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Colon and Rectum)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a7) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b7) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c7) Minimal (n=521)	--		--	--	
d7) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Kidney and Bladder)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a8) Minimal (n=521)	Low	130	0.0	0.64 (0.23,1.83)	0.368
	Medium	260	1.5		
	High	131	0.0		
b8) Maximal (n=742)	Low	185	0.5	0.86 (0.43,1.73)	0.673
	Medium	371	1.1		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c8) Minimal (n=521)	0.75 (0.26,2.21)		0.583	AGE (p=0.095)	
d8) Maximal (n=742)	0.86 (0.43,1.73)		0.673	--	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Prostate)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a9) Minimal (n=521)	Low	130	0.0	0.64 (0.15,2.82)	0.522
	Medium	260	0.8		
	High	131	0.0		
b9) Maximal (n=742)	Low	185	0.0	1.04 (0.39,2.81)	0.933
	Medium	371	0.5		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c9) Minimal (n=521)	--		--	--	
d9) Maximal (n=742)	--		--	--	

^aRelative risk for a twofold increase in dioxin.

--: Adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Testicles)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a10) Minimal (n=521)	Low	130	0.8	0.59 (0.17,2.09)	0.363
	Medium	260	0.8		
	High	131	0.0		
b10) Maximal (n=742)	Low	185	0.0	1.00 (0.44,2.30)	0.999
	Medium	371	0.8		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c10) Minimal (n=521)	0.59 (0.17,2.09)		0.363	--	
d10) Maximal (n=742)	1.00 (0.44,2.30)		0.999	--	

^aRelative risk for a twofold increase in dioxin.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Ill-Defined Sites)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a11) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b11) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c11) Minimal (n=521)	--		--	--	
d11) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Carcinoma in Situ of Penis)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted						
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value	
a12) Minimal (n=521)	Low	130	0.0	--	--	
	Medium	260	0.0			
	High	131	0.0			
b12) Maximal (n=742)	Low	185	0.0	--	--	
	Medium	371	0.0			
	High	186	0.0			
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted						
Assumption				Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c12) Minimal (n=521)				--	--	--
d12) Maximal (n=742)				--	--	--

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Carcinoma in Situ of Other and Unspecified Sites)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a13) Minimal (n=521)	Low	130	0.8	--	--
	Medium	260	0.0		
	High	131	0.0		
b13) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.3		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c13) Minimal (n=521)	--		--	--	
d13) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Hodgkin's Disease)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a14) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.0		
	High	131	0.0		
b14) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.0		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c14) Minimal (n=521)	--		--	--	
d14) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.
Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Leukemia)

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
a15) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.4		
	High	131	0.0		
b15) Maximal (n=742)	Low	185	0.0	--	--
	Medium	371	0.3		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c15) Minimal (n=521)	--		--	--	
d15) Maximal (n=742)	--		--	--	

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue)**

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a16) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.4		
	High	131	0.0		
b16) Maximal (n=742)	Low	185	0.0	0.84 (0.27,2.57)	0.745
	Medium	371	0.5		
	High	186	0.0		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
c16) Minimal (n=521)	--		--	--	
d16) Maximal (n=742)	--		--	--	

^aRelative risk for a twofold increase in dioxin.

--: Relative risk, confidence interval, and p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Ear, Face, Head, and Neck)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e1) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f1) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
g1) Minimal (n=521)	≤18.6	--		--	--	
	>18.6	--		--	--	
h1) Maximal (n=742)	≤18.6	--		--	--	
	>18.6	--		--	--	

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Oral Cavity, Pharynx, and Larynx)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e2) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f2) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g2) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h2) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Brain)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e3) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f3) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g3) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h3) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Thymus and Mediastinum)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e4) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f4) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted					
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks	
g4) Minimal (n=521)	≤18.6	--	--	--	
	>18.6	--	--	--	
h4) Maximal (n=742)	≤18.6	--	--	--	
	>18.6	--	--	--	

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Thyroid Gland)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e5) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f5) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g5) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h5) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Bronchus and Lung)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e6) Minimal (n=521)	≤18.6	0.0 (72)	0.8 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f6) Maximal (n=742)	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted					
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate	Remarks
g6) Minimal (n=521)	≤18.6	--	--	--	--
	>18.6	--	--	--	--
h6) Maximal (n=742)	≤18.6	--	--	--	--
	>18.6	--	--	--	--

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Colon and Rectum)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e7) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f7) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g7) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h7) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Kidney and Bladder)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e8) Minimal (n=521)	≤18.6	0.0 (72)	0.8 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	2.3 (132)	0.0 (77)	0.45 (0.10,1.94)	0.281 ^b
f8) Maximal (n=742)	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	--	--
	>18.6	1.3 (79)	1.7 (179)	0.0 (104)	0.67 (0.27,1.62)	0.372 ^b

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) ^a	p-Value	Covariate Remarks
g8) Minimal (n=521)	≤18.6	--	--	AGE (p=0.149)
	>18.6	0.56 (0.13,2.41)	0.435 ^b	
h8) Maximal (n=742)	≤18.6	--	--	--
	>18.6	0.67 (0.27,1.62)	0.372 ^b	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Prostate)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	<u>Percent Yes/(n)</u> Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e9) Minimal (n=521)	≤18.6	0.0 (72)	0.8 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	0.0 (77)	--	--
f9) Maximal (n=742)	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.6 (179)	0.0 (104)	--	--
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)		p-Value	Covariate Remarks	
g9) Minimal (n=521)	≤18.6	--		--	--	
	>18.6	--		--	--	
h9) Maximal (n=742)	≤18.6	--		--	--	
	>18.6	--		--	--	

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Testicles)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	<u>Percent Yes/(n) Current Dioxin</u>			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e10) Minimal						--
(n=521)	≤18.6	1.4 (72)	0.8 (128)	0.0 (54)	0.63 (0.12,3.29)	0.581 ^b
	>18.6	0.0 (58)	0.8 (132)	0.0 (77)	--	--
f10) Maximal						--
(n=742)	≤18.6	0.0 (106)	1.0 (191)	0.0 (83)	1.13 (0.39,3.28)	0.828 ^b
	>18.6	0.0 (79)	0.6 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g10) Minimal			--	--
(n=521)	≤18.6	--	--	
	>18.6	--	--	
h10) Maximal			--	--
(n=742)	≤18.6	--	--	
	>18.6	--	--	

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Ill-Defined Sites)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e11) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f11) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g11) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h11) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Carcinoma in Situ of Penis)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e12) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f12) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g12) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h12) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Carcinoma in Situ of Other and Unspecified Sites)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e13) Minimal (n=521)	≤18.6	1.4 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f13) Maximal (n=742)	≤18.6	0.0 (106)	0.5 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g13) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h13) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Hodgkin's Disease)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e14) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.0 (132)	0.0 (77)	--	--
f14) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.0 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g14) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h14) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Leukemia)

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
e15) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	0.0 (77)	--	--
f15) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (79)	0.6 (179)	0.0 (104)	--	--

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted				
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g15) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h15) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue)**

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.) ^a	p-Value
		Low	Medium	High		
e16) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	0.0 (77)	--	--
f16) Maximal (n=742)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	1.3 (79)	0.6 (179)	0.0 (104)	0.46 (0.09,2.26)	0.338 ^b

Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
g16) Minimal (n=521)	≤18.6	--	--	--
	>18.6	--	--	--
h16) Maximal (n=742)	≤18.6	--	--	--
	>18.6	--	--	--

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: **Minimal**--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.
Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Ear, Face, Head, and Neck)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.1	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	0.999
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Oral Cavity, Pharynx, and Larynx)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.1	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	0.999
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Brain)

i3) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	--
Low	196	0.0	Low vs. Background	--	--
High	187	0.0	High vs. Background	--	--
Total	1,514				

j3) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Thymus and Mediastinum)**

i4) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.3	Unknown vs. Background	--	0.610
Low	196	0.0	Low vs. Background	--	--
High	187	0.0	High vs. Background	--	--
Total	1,514				

j4) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Thyroid Gland)**

i5) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	--
Low	196	0.0	Low vs. Background	--	--
High	187	0.0	High vs. Background	--	--
Total	1,514				

j5) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Bronchus and Lung)**

i6) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.6	Unknown vs. Background	--	0.186
Low	196	0.5	Low vs. Background	--	0.400
High	187	0.0	High vs. Background	--	--
Total	1,514				

j6) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Colon and Rectum)**

i7) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.3	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	0.999
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j7) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Kidney and Bladder)**

i8) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.3	All Categories		0.006
Unknown	345	0.3	Unknown vs. Background	1.14 (0.10,12.61)	0.999
Low	196	2.0	Low vs. Background	8.17 (1.49,44.91)	0.033
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j8) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.041	AGE (p=0.036)
Unknown	345	Unknown vs. Background	1.13 (0.10,12.55)	0.923	
Low	196	Low vs. Background	8.60 (1.55,47.71)	0.014	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.
 Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Prostate)**

i9) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.5	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	0.466
Low	196	1.0	Low vs. Background	2.02 (0.37,11.08)	0.688
High	187	0.0	High vs. Background	--	0.850
Total	1,514				

j9) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	AGE (p<0.001)
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	2.28 (0.40,12.96)	0.353	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Testicles)**

i10) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	--
Low	196	1.0	Low vs. Background	--	0.079
High	187	0.0	High vs. Background	--	--
Total	1,514				

j10) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(III-Defined Sites)

i11) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	--
Low	196	0.0	Low vs. Background	--	--
High	187	0.0	High vs. Background	--	--
Total	1,514				

j11) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Carcinoma in Situ of Penis)**

i12) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.1	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	0.999
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j12) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3$ ppt.
 High (Ranch Hands): Current Dioxin > 33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Carcinoma in Situ on Other and Unspecified Sites)**

i13) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	--
Low	196	0.0	Low vs. Background	--	--
High	187	0.0	High vs. Background	--	--
Total	1,514				

j13) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the absence of abnormalities; adjusted analysis not performed due to the absence of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Hodgkin's Disease)**

i14) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.1	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	0.999
Low	196	0.0	Low vs. Background	--	0.999
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j14) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)
Analysis of Malignant Systemic Neoplasms
(Leukemia)

i15) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.0	All Categories		--
Unknown	345	0.0	Unknown vs. Background	--	--
Low	196	0.5	Low vs. Background	--	0.400
High	187	0.0	High vs. Background	--	--
Total	1,514				

j15) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		--	--
Unknown	345	Unknown vs. Background	--	--	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities; adjusted analysis not performed due to the sparse number of abnormalities.

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-18. (Continued)

**Analysis of Malignant Systemic Neoplasms
(Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue)**

i16) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	0.1	All Categories		0.641
Unknown	345	0.3	Unknown vs. Background	2.28 (0.14,36.59)	0.999
Low	196	0.5	Low vs. Background	4.03 (0.25,64.65)	0.720
High	187	0.0	High vs. Background	--	0.999
Total	1,514				

j16) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	786	All Categories		0.687	AGE (p=0.088)
Unknown	345	Unknown vs. Background	2.30 (0.14,37.13)	0.558	
Low	196	Low vs. Background	4.27 (0.26,69.08)	0.307	
High	187	High vs. Background	--	--	
Total	1,514				

--: Relative risk/confidence interval/p-value not given due to the sparse number of abnormalities.
 Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin ≤ 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under the minimal and maximal assumptions, no Ranch Hands had a verified malignant systemic neoplasm for the ear, face, head, and neck (Table 7-18 [e1-h1]); oral cavity, pharynx, and larynx (Table 7-18 [e2-h2]); brain (Table 7-18 [e3-h3]); thymus and mediastinum (Table 7-18 [e4-h4]); thyroid gland (Table 7-18 [e5-h5]); colon and rectum (Table 7-18 [e7-h7]); ill-defined sites (Table 7-18 [e11-h11]); carcinoma in situ of penis (Table 7-18 [e12-h12]); and Hodgkin's disease (Table 7-18 [e14-h14]).

Under the minimal and maximal assumptions, only one Ranch Hand had a verified malignant systemic neoplasm of the bronchus and lung (Table 7-18 [e6-h6]); carcinoma in situ of other and unspecified sites (Table 7-18 [e13-h13]); and leukemia (Table 7-18 [e15-h15]).

Under the minimal assumption, four Ranch Hands had a verified malignant systemic neoplasm of the kidney and bladder. One Ranch Hand was in the later tour stratum (i.e., ≤ 18.6 years) and three Ranch Hands were in the earlier tour stratum (i.e., > 18.6 years). Due to the sparse data in the later tour stratum, the relative risk was not evaluated for that stratum nor was the interaction between current dioxin and time since tour evaluated. For the earlier tour stratum, the relative risks were less than 1 and nonsignificant under both the minimal and the maximal assumptions (Table 7-18 [e8] and [f8]: $p=0.281$ and $p=0.372$). In the adjusted analyses, age was the only covariate considered due to the sparse data. Under the minimal assumption, the adjusted relative risk for the earlier tour stratum was less than 1 and nonsignificant (Table 7-18 [g8]: $p=0.435$). Under the maximal assumption, age was not retained as a covariate; therefore, the unadjusted and adjusted results were the same (Table 7-18 [f8] and [h8]).

Under the minimal assumption and under the maximal assumption, the two Ranch Hands with a verified malignant systemic neoplasm of the prostate were split between the time strata. Because of the sparse number of neoplasms within each time stratum, only relative frequencies and sample sizes were presented (Table 7-18 [e9-h9]).

Under the minimal and maximal assumptions, three Ranch Hands had a verified malignant systemic neoplasm of the testicles. Two of the three Ranch Hands had later tours (≤ 18.6 years). Under both assumptions, the relative risk for that time stratum was nonsignificant (Table 7-18 [e10] and [f10]: $p=0.581$ and $p=0.828$). Neither the interaction of current dioxin and time since tour nor the relative risk of the other time stratum was evaluated for significance. Because of the sparse data, adjusted analyses were not performed.

Under the minimal assumption, only one Ranch Hand within the earlier tour stratum (> 18.6 years) had a verified malignant systemic neoplasm of lymphoid and histiocytic tissue. Therefore, only relative frequencies and sample sizes are presented (Table 7-18 [e16]). Under the maximal assumption, two Ranch Hands had verified malignant systemic neoplasm of lymphoid and histiocytic tissue within the earlier tour stratum; the associated relative risk was nonsignificant and less than 1 (Table 7-18 [f16]: $p=0.338$). Due to sparse data, the interaction and other time stratum were not evaluated for significance and adjusted analyses were not performed.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

No Ranch Hands and no Comparisons had a verified malignant systemic neoplasm of the brain (Table 7-18 [i3-j3]); thyroid gland (Table 7-18 [i5-j5]), ill-defined sites (Table 7-18 [i11-j11]); and carcinoma in situ of other and unspecified sites (Table 7-18 [i13-j13]).

One Comparison and no Ranch Hands had a verified systemic neoplasm for the ear, face, head, and neck (Table 7-18 [i1-j1]); oral cavity, pharynx, and larynx (Table 7-18 [i2-j2]); carcinoma in situ of the penis (Table 7-18 [i12-j12]); and Hodgkin's disease (Table 7-18 [i14-j14]). Each of the Ranch Hand versus Comparison contrasts was nonsignificant.

Only one Ranch Hand in the unknown current dioxin category had a verified malignant systemic neoplasm of the thymus and mediastinum (Table 7-18 [i4-j4]). The associated Ranch Hand versus Comparison contrast was nonsignificant ($p=0.610$).

Two Ranch Hands in the unknown current dioxin category and one Ranch Hand in the low current dioxin category had a verified malignant systemic neoplasm of the bronchus and lung (Table 7-18 [i6-j6]). The unknown versus background and the low versus background contrasts were nonsignificant in the unadjusted analysis ($p>0.15$ for both contrasts).

Two Comparisons in the background current dioxin category and no Ranch Hands had a verified malignant systemic neoplasm of the colon and rectum (Table 7-18 [i7-j7]). Each of the Ranch Hand versus Comparison contrasts was nonsignificant ($p=0.999$) in the unadjusted analysis.

Two Comparisons, one Ranch Hand in the unknown current dioxin category, and four Ranch Hands in the low current dioxin category had a verified malignant systemic neoplasm of the kidney and bladder. In the unadjusted analysis, the overall contrast of the relative frequencies was significant (Table 7-18 [i8]: $p=0.006$). The relative frequencies of participants with a malignant systemic neoplasm of the kidney and bladder were 0.3, 0.3, 2.0, and 0.0 percent for the background, unknown, low, and high current dioxin categories. The contrast of Ranch Hands in the low current dioxin category with Comparisons in the background category was significant with a relative risk greater than 1 (Est. RR=8.17, 95% C.I.: [1.49,44.91], $p=0.033$). The other two Ranch Hand versus Comparison contrasts were nonsignificant ($p=0.999$ for both). An adjusted analysis also contained a significant overall contrast (Table 7-18 [j8]: $p=0.041$). The low versus background contrast remained significant after adjusting for age (Adj. RR=8.60, 95% C.I.: [1.55, 47.71], $p=0.014$). The unknown versus background contrast was nonsignificant ($p=0.923$).

Four Comparisons in the background current dioxin category and two Ranch Hands in the low current dioxin category had a verified malignant systemic neoplasm of the prostate (Table 7-18 [i9-j9]). In the unadjusted analysis, the three Ranch Hand versus Comparison contrasts for malignant systemic neoplasms were nonsignificant ($p>0.45$ for each contrast). An adjusted analysis with age in the model provided a nonsignificant low versus background contrast (Table 7-18 [j9]: $p=0.353$).

Only two Ranch Hands in the low current dioxin category had a verified malignant systemic neoplasm of the testicles (Table 7-18 [i10-j10]). The individual contrast of low versus background was of borderline significance ($p=0.079$).

One Ranch Hand in the low current dioxin category had a verified leukemia (Table 7-18 [i15-j15]). The contrast of low versus background was nonsignificant ($p=0.400$) in the unadjusted analysis.

One Comparison, one Ranch Hand in the unknown current dioxin category, and one Ranch Hand in the low current dioxin category had a malignant systemic neoplasm of lymphoid and histiocytic tissue (Table 7-18 [i16]). In the unadjusted analysis, the overall contrast and the individual contrasts of the relative frequencies of Ranch Hands in the unknown, low, and high current dioxin categories versus Comparisons in the background category were nonsignificant ($p>0.60$ for all). The adjusted analysis also produced a nonsignificant overall contrast ($p=0.687$).

All Skin and Systemic Neoplasms

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In the unadjusted analysis of the frequency of verified skin and systemic neoplasms combined, the relative risk associated with initial dioxin was nonsignificant under the minimal and maximal assumptions (Table 7-19 [a] and [b]: $p=0.384$ and $p=0.661$). The adjusted analyses also produced nonsignificant relative risks (Table 7-19 [c] and [d]: $p=0.851$ and $p=0.285$, respectively).

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

In the unadjusted analysis of the frequency of verified skin and systemic neoplasms combined, the interaction between current dioxin and time since tour was nonsignificant under the minimal and maximal assumptions (Table 7-19 [e] and [f]: $p=0.414$ and $p=0.355$). Under both assumptions, the adjusted analysis also contained a nonsignificant interaction (Table 7-19 [g] and [h]: $p=0.625$ and $p=0.387$, respectively). Associations with current dioxin were nonsignificant within each time stratum.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis of the frequency of participants with a verified skin or systemic neoplasm, the overall contrast of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category was nonsignificant (Table 7-19 [i1]: $p=0.679$). An adjusted analysis also exhibited a nonsignificant overall contrast (Table 7-19 [j1]: $p=0.576$). The overall contrast of the unadjusted analysis remained nonsignificant after including suspected neoplasms (Table 7-19 [i2]: $p=0.730$), as did the overall contrast in the adjusted analysis for verified and suspected neoplasms combined (Table 7-19 [j2]: $p=0.629$). In the unadjusted and the adjusted analyses for the verified neoplasms, as well as the verified and suspected neoplasms, the individual Ranch Hand versus Comparison contrasts had relative risks greater than 1 but they were all nonsignificant ($p>0.20$ for all).

TABLE 7-19.

Analysis of All Skin and Systemic Neoplasms

Ranch Hands - Log₂ (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Yes	Est. Relative Risk (95% C.I.)^a	p-Value
a) Minimal (n=521)	Low	130	26.2	0.93 (0.78,1.10)	0.384
	Medium	260	21.9		
	High	131	24.4		
b) Maximal (n=742)	Low	185	17.8	1.03 (0.91, 1.17)	0.661
	Medium	371	24.3		
	High	186	21.5		
Ranch Hands - Log₂ (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
c) Minimal (n=515)	0.98 (0.82,1.18)		0.851	AGE (p=0.004) CARCIN (p=0.022)	
d) Maximal (n=731)	1.08 (0.94,1.23)		0.285	AGE (p<0.001) CARCIN (p=0.033)	

^aRelative risk for a twofold increase in dioxin.

Note: **Minimal**--Low: 52-93 ppt; Medium: >93-292 ppt; High: >292 ppt.

Maximal--Low: 25-56.9 ppt; Medium: >56.9-218 ppt; High: >218 ppt.

TABLE 7-19. (Continued)

Analysis of All Skin and Systemic Neoplasms

Ranch Hands - Log₂ (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Yes/(n) Current Dioxin			Est. Relative Risk (95% C.I.)^a	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	26.4 (72)	22.7 (128)	18.5 (54)	0.82 (0.61,1.10)	0.414 ^b 0.187 ^c
	>18.6	27.6 (58)	21.2 (132)	27.3 (77)	0.96 (0.77,1.20)	0.703 ^c
f) Maximal (n=742)	≤18.6	20.8 (106)	24.6 (191)	16.9 (83)	0.95 (0.78,1.16)	0.355 ^b 0.618 ^c
	>18.6	16.5 (79)	22.9 (179)	25.0 (104)	1.08 (0.91,1.28)	0.402 ^c
Ranch Hands - Log₂ (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.)^a		p-Value	Covariate Remarks	
g) Minimal (n=515)	≤18.6	0.92 (0.68,1.25)		0.625 ^b 0.579 ^c	AGE (p=0.008) CARCIN (p=0.024)	
	>18.6	1.01 (0.80,1.27)		0.953 ^c		
h) Maximal (n=731)	≤18.6	1.02 (0.82,1.26)		0.387 ^b 0.872 ^c	AGE (p<0.001) CARCIN (p=0.036)	
	>18.6	1.15 (0.96,1.37)		0.132 ^c		

^aRelative risk for a twofold increase in dioxin.

^bTest of significance for homogeneity of relative risks (current dioxin continuous, time categorized).

^cTest of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.

Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 7-19. (Continued)

**Analysis of All Skin and Systemic Neoplasms
(Verified)**

i1) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	19.6	All Categories		0.679
Unknown	345	20.6	Unknown vs. Background	1.06 (0.78,1.46)	0.702
Low	196	23.5	Low vs. Background	1.26 (0.87,1.83)	0.230
High	187	21.4	High vs. Background	1.12 (0.76,1.65)	0.580
Total	1,514				

j1) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.576	AGE (p<0.001) CARCIN (p=0.125)
Unknown	340	Unknown vs. Background	1.05 (0.77,1.44)	0.757	
Low	193	Low vs. Background	1.24 (0.84,1.81)	0.276	
High	185	High vs. Background	1.25 (0.84,1.87)	0.267	
Total	1,497				

Note: Background (Comparisons): Current Dioxin \leq 10 ppt.
 Unknown (Ranch Hands): Current Dioxin \leq 10 ppt.
 Low (Ranch Hands): 15 ppt < Current Dioxin \leq 33.3 ppt.
 High (Ranch Hands): Current Dioxin >33.3 ppt.

TABLE 7-19. (Continued)

**Analysis of All Skin and Systemic Neoplasms
(Verified and Suspected)**

i2) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Yes	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	786	19.8	All Categories		0.730
Unknown	345	20.6	Unknown vs. Background	1.05 (0.76,1.43)	0.777
Low	196	23.5	Low vs. Background	1.24 (0.85,1.80)	0.263
High	187	21.4	High vs. Background	1.10 (0.74,1.63)	0.636
Total	1,514				

j2) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.629	AGE (p<0.001) CARCIN (p=0.143)
Unknown	340	Unknown vs. Background	1.03 (0.75,1.42)	0.833	
Low	193	Low vs. Background	1.22 (0.83,1.78)	0.313	
High	185	High vs. Background	1.23 (0.83,1.84)	0.303	
Total	1,497				

Note: Background (Comparisons): Current Dioxin ≤ 10 ppt.
 Unknown (Ranch Hands): Current Dioxin ≤ 10 ppt.
 Low (Ranch Hands): $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$.
 High (Ranch Hands): Current Dioxin $> 33.3 \text{ ppt}$.

DISCUSSION

In ambulatory medicine, the recommendation that asymptomatic individuals undergo periodic physical examinations is based largely on the assumption that such screening will reveal occult malignancy. Although the guidelines for the frequency and content of such examinations are subject to debate, there is no doubt that early detection affords the best and, in most forms of cancer, the only chance for cure. While no one screening test is absolutely reliable, the scope and depth of the protocol employed in this longitudinal study far exceed what would be considered routine in clinical practice.

As the anatomic point of contact with industrial toxins and as the only organ system with a clearly defined clinical endpoint (chloracne) for TCDD exposure, the skin deserves the special emphasis it has received in this study. Though there is no other epidemiologic evidence that TCDD exposure causes—or that chloracne is associated with—basal cell carcinoma, an increased incidence of these skin cancers in the Ranch Hand cohort has been documented in each of the three physical examination cycles.

At the Baseline examination, a significantly higher rate of verified basal cell carcinoma was found in the Ranch Hand cohort in the unadjusted analysis. After the Baseline, heightened efforts were made to clarify the contribution of risk factors such as cumulative sun exposure; skin tannability; eye, skin, and hair color; parental ethnicity; and lifetime cigarette smoking history. In the 1985 examination, the adjusted analysis of verified basal cell carcinoma again displayed a significant group difference. In the 1987 examination, which included biopsies from 19 Ranch Hands and 20 Comparisons, the adjusted group contrast for the verified basal cell carcinoma history was significant ($p=0.030$); the adjusted group contrast for the verified and suspected set of basal cell carcinomas was marginally significant ($p=0.053$). In contrast to the significant group differences reported for the 1985 and 1987 examinations, the relative risks for basal cell carcinoma and sun exposure-related malignant skin neoplasms often were less than 1 in these serum dioxin analyses.

With reference to systemic neoplasms, the frequency of systemic cancer in Ranch Hands and Comparisons was similar for the 1987 examination of AFHS. Though the statistical power for detecting group differences in the incidence of specific rare systemic neoplasms is low, the Ranch Hand and Comparison group frequencies have not differed over time and no significant group differences in cancer-related mortality have been found. For the 1985 examination, one Ranch Hand and one Comparison had verified STS (fibrous histiocytoma and fibrosarcoma, respectively). The Ranch Hand was not part of the 1987 study because he died; the Comparison with the fibrosarcoma was part of the 1987 examination. At the 1985 examination, one Ranch Hand was classified as having suspected leukemia, HD, or NHL. He was diagnosed as a verified leukemia by the time of the 1987 examination. At the 1987 examination, there was one verified case of NHL in a Ranch Hand.

In the current report, the data analyzed can be divided into two broad categories: cutaneous and systemic neoplasms of benign or malignant nature. Except for the occupation-specific analyses, there was no increased risk for the development of any malignant skin neoplasm related to the body burden of dioxin. The analyses by occupation were performed because different occupational duties resulted in different degrees of exposure. In association with the current and extrapolated initial levels of serum dioxin, a statistically significant increase in the incidence of basal cell skin cancers of other sites (excluding ear, face, head,

and neck) was noted in the enlisted flyer category but not in the enlisted groundcrew category, which, on the whole, was more heavily exposed to TCDD. Furthermore, in a pattern consistent with a dose-response effect, a significantly higher incidence (4/32, 12.5%) of basal cell skin cancers was noted in Ranch Hand enlisted flyers with high levels of serum dioxin ($p=0.020$) when contrasted with Comparisons (1/108, 0.9%); a higher but nonsignificant incidence also was found for Ranch Hands with low levels (1/50, 2.0%) versus Comparisons. The importance of these positive associations is uncertain, however, because the isolated findings were limited to one occupational cohort.

In the analysis of systemic neoplasms, a few statistically significant positive associations were found; however, this was due to an increased incidence of benign (but not malignant) neoplasms in the Ranch Hand group. Lipomas are one example of a benign systemic neoplasm. Under the maximal assumption, in a pattern consistent with a dose-response, Ranch Hand participants with high levels of extrapolated initial serum dioxin had a greater incidence (9.7%) of benign systemic neoplasms than did Ranch Hands with medium or low levels (5.7% and 1.6%). In the adjusted analysis, the relative risk remained significant ($p<0.001$). In the analysis of current serum dioxin by time since tour, this positive association was stronger in participants with more than 18.6 years since service in SEA. Furthermore, Ranch Hands with the highest levels of current serum dioxin (>33.3 ppt) had a significantly higher incidence (10.2%) of benign systemic neoplasms ($p=0.043$) versus the Comparisons (4.1%).

In contrast, there was no evidence for any positive association between the current or extrapolated initial body burden of dioxin and the incidence of any malignant systemic neoplasm. Relative to the Comparisons (1.7%), Ranch Hands with low serum dioxin levels (15 ppt to 33.3 ppt) had a significantly higher frequency (5.1%) of malignant systemic neoplasms ($p=0.016$), but Ranch Hands with high serum dioxin (over 33.3 ppt) had a lower frequency (0.0%) that was not significant ($p=0.122$). The study provides no evidence of increased incidence for the neoplasms most commonly associated with exposure to chlorophenols (HD, NHL, and STS). However, the number of participants with these specific neoplasms was very small; therefore, the statistical power to detect relative risks and group differences was low.

In summary, the increased incidence of basal cell skin cancers in Ranch Hands documented in previous examination cycles was not associated significantly with serum dioxin, except within the enlisted flyers at sites other than ear, face, head, and neck. In the analysis of systemic neoplasms, in a pattern consistent with a dose-response, an increased incidence of benign neoplasms was noted in the Ranch Hand cohort, particularly in those participants most removed from Vietnam. Finally, relative to the Comparisons, there was no increased incidence of any malignant systemic neoplasm in Ranch Hands with the highest serum dioxin levels.

SUMMARY

For the malignancy assessment, Tables 7-20, 7-21, and 7-22 summarize the results from analyses based on initial dioxin, current dioxin and time since tour, and categorized current dioxin. All variables were discrete.

TABLE 7-20.

Summary of Initial Dioxin Analyses for Malignancy Variables
Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
Skin Neoplasms				
<u>Behavior</u>				
All	-0.014	ns*	-0.021	ns
Malignant	-0.014	ns	** (ns)	ns
Benign (Non-Blacks Only)	ns	ns	ns	ns
Benign (Blacks Included)	ns	ns	ns	ns
Uncertain Behavior or Unspecified Nature	--	--	--	--
<u>Cell Type</u>				
Basal Cell Carcinoma				
All Sites Combined	-0.037	ns	ns	ns
Ear, Face, Head, and Neck	-0.002	-0.017	-0.025	ns*
Trunk	ns	NS	NS	NS
Upper Extremities	ns	ns	--	ns
Lower Extremities	--	--	--	--
Other Sites and NOS	NS	NS	NS	NS
Sun Exposure-Related Malignant Skin Neoplasms				
All Sites Combined	-0.014	ns	** (ns)	ns
Ear, Face, Head, and Neck	-0.003	-0.031	-0.047	ns
Trunk	ns	ns	ns	ns
Upper Extremities	NS	ns	--	ns
Lower Extremities	--	--	--	--
Other Sites and NOS	NS	NS	NS	NS

TABLE 7-20. (Continued)

Summary of Initial Dioxin Analyses for Malignancy Variables
Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
Melanoma				
All Sites Combined	--	ns	--	--
Ear, Face, Head, and Neck	--	--	--	--
Trunk	-0.011	ns	--	--
Upper Extremities	--	--	--	--
Lower Extremities	--	--	--	--
Other Sites and NOS	--	--	--	--
Squamous Cell Carcinoma	ns	NS	ns	NS
<u>Basal Cell Carcinoma by Occupation</u>				
Officer -				
Ear, Face, Head, and Neck vs. None	NS	NS	NS	NS
Officer -				
Other Sites vs. None	--	ns	--	ns
Enlisted Flyer -				
Ear, Face, Head, and Neck vs. None	ns	ns	ns	ns
Enlisted Flyer -				
Other Sites vs. None	+0.050	+0.015	NS	+0.039
Enlisted Groundcrew -				
Ear, Face, Head, and Neck vs. None	-0.005	ns*	-0.021	ns
Enlisted Groundcrew -				
Other Sites vs. None	ns*	ns	ns	ns

TABLE 7-20. (Continued)

**Summary of Initial Dioxin Analyses for Malignancy Variables
Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
<u>Sun Exposure-Related</u>				
<u>Malignant Skin</u>				
<u>Neoplasm by Occupation</u>				
Officer -				
Ear, Face, Head, and				
Neck vs. None	ns	NS	ns	NS
Officer -				
Other Sites vs. None	ns	ns	ns	ns
Enlisted Flyer -				
Ear, Face, Head, and				
Neck vs. None	ns	ns	ns	ns
Enlisted Flyer -				
Other Sites vs. None	NS*	+0.015	NS	+0.049
Enlisted Groundcrew -				
Ear, Face, Head, and				
Neck vs. None	-0.022	ns	ns*	ns
Enlisted Groundcrew -				
Other Sites vs. None	ns*	ns	ns	ns
<u>Basal Cell Carcinoma</u>				
<u>(Number)</u>				
One vs. None	ns	ns	ns	ns
Multiple vs. None	-0.026	ns	ns	ns
Systemic Neoplasms				
All	NS	+0.009	NS	+0.006
Malignant	-0.048	ns	ns	ns
Benign	+0.022	+0.001	+0.015	+<0.001
Uncertain Behavior				
or Unspecified Nature	ns	NS	ns	NS
<u>Malignant Systemic Neoplasms</u>				
<u>by Location/Site</u>				
Ear, Face, Head, and Neck	--	--	--	--
Oral Cavity, Pharynx, and				
Larynx	--	--	--	--

TABLE 7-20. (Continued)

Summary of Initial Dioxin Analyses for Malignancy Variables
Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	Unadjusted		Adjusted	
	Minimal	Maximal	Minimal	Maximal
<u>Malignant Systemic Neoplasms</u>				
<u>by Location/Site (continued)</u>				
Brain	--	--	--	--
Thymus and Mediastinum	--	--	--	--
Thyroid Gland	--	--	--	--
Bronchus and Lung	--	--	--	--
Colon and Rectum	--	--	--	--
Kidney and Bladder	ns	ns	ns	ns
Prostate	ns	NS	--	--
Testicles	ns	NS	ns	NS
Ill-Defined Sites	--	--	--	--
Carcinoma In Situ of Penis	--	--	--	--
Carcinoma In Situ of Other and Unspecified Sites	--	--	--	--
Hodgkin's Disease	--	--	--	--
Leukemia	--	--	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	--	ns	--	--
Skin and Systemic Neoplasms				
All	ns	NS	ns	NS

+: Relative risk 1.00 or greater.

-: Relative risk less than 1.00.

NS/ns: Not significant ($p > 0.10$).

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

--: Analysis not performed due to sparse data.

** (ns): Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); not significant when interaction is deleted; refer to Table F-1 for a detailed description of this interaction.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

TABLE 7-21.

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	C*T	Unadjusted		C*T	Maximal	
		Minimal			Maximal	
		≤18.6	>18.6		≤18.6	>18.6
Skin Neoplasms						
Behavior						
All	NS	ns*	ns*	NS	ns*	ns
Malignant	NS	-0.046	ns	NS	ns	ns
Benign (Non-Blacks only)	NS	ns	ns	NS	ns	NS
Benign (Blacks Included)	NS	ns	ns	NS	ns	NS
Uncertain Behavior or Unspecified Nature	--	--	--	--	--	--
Cell Type						
Basal Cell Carcinoma						
All Sites Combined	ns	ns	ns	NS	ns	ns
Ear, Face, Head, and Neck	ns	ns	-0.011	ns	ns	ns*
Trunk	ns	ns	ns	NS	ns	NS
Upper Extremities	--	--	--	--	--	ns
Lower Extremities	--	--	--	--	--	--
Other Sites and NOS	--	--	NS	--	--	NS
Sun Exposure-Related Malignant Skin Neoplasms						
All Sites Combined	NS	ns*	ns	NS	ns	ns
Ear, Face, Head, and Neck	ns	ns*	-0.029	ns	ns	ns
Trunk	NS	ns	ns	NS	ns	ns
Upper Extremities	--	--	NS	--	--	ns
Lower Extremities	--	--	--	--	--	--
Other Sites and NOS	--	--	NS	--	--	NS

TABLE 7-21. (Continued)

Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	Unadjusted					
	C*T	Minimal		C*T	Maximal	
		≤18.6	>18.6		≤18.6	>18.6
Melanoma						
All Sites Combined	--	--	--	--	--	ns
Ear, Face, Head, and Neck	--	--	--	--	--	--
Trunk	--	--	--	--	--	--
Upper Extremities	--	--	--	--	--	--
Lower Extremities	--	--	--	--	--	--
Other Sites and NOS	--	--	--	--	--	--
Squamous Cell Carcinoma	--	ns	--	--	ns	--
Basal Cell Carcinoma by Occupation						
Officer -						
Ear, Face, Head, and Neck vs. None	NS	ns	ns	NS	NS	NS
Officer -						
Other Sites vs. None	--	--	--	NS	ns	ns
Enlisted Flyer -						
Ear, Face, Head, and Neck vs. None	--	NS	--	--	ns	--
Enlisted Flyer -						
Other Sites vs. None	+0.011	NS	+0.037	+0.017	NS	+0.037
Enlisted Groundcrew -						
Ear, Face, Head, and Neck vs. None	NS	ns*	-0.047	NS	ns*	ns
Enlisted Groundcrew -						
Other Sites vs. None	ns	ns	ns	NS	ns	ns

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	Unadjusted					
	C*T	Minimal		C*T	Maximal	
		≤18.6	>18.6		≤18.6	>18.6
<u>Sun Exposure-Related</u>						
<u>Malignant Skin</u>						
<u>Neoplasm by Occupation</u>						
Officer -						
Ear, Face, Head, and						
Neck vs. None	NS	ns	ns	ns	NS	NS
Officer -						
Other Sites vs. None	--	--	ns	NS	ns	ns
Enlisted Flyer -						
Ear, Face, Head, and						
Neck vs. None	--	ns	--	--	ns	--
Enlisted Flyer -						
Other Sites vs. None	+0.010	NS	+0.037	+0.017	NS	+0.038
Enlisted Groundcrew -						
Ear, Face, Head, and						
Neck vs. None	NS	ns*	ns	NS	ns*	ns
Enlisted Groundcrew -						
Other Sites vs. None	NS	ns	ns	NS	ns	ns
<u>Basal Cell Carcinoma</u>						
<u>(Number)</u>						
One vs. None	NS	ns	ns	ns	ns	ns
Multiple vs. None	ns	ns	ns	NS	ns	ns
Systemic Neoplasms						
All	NS	ns	NS	ns	NS	NS*
Malignant	ns	ns	ns	ns	NS	ns
Benign	NS	NS	+0.035	NS	NS*	+0.013
Uncertain Behavior						
or Unspecified Nature	--	--	ns	--	--	NS
<u>Malignant Systemic Neoplasms</u>						
<u>by Location/Site</u>						
Ear, Face, Head, and						
Neck	--	--	--	--	--	--
Oral Cavity, Pharynx,						
and Larynx	--	--	--	--	--	--

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	Unadjusted					
	C*T	Minimal		Maximal		
		≤18.6	>18.6	C*T	≤18.6	>18.6
<u>Malignant Systemic Neoplasms</u>						
<u>by Location/Site (continued)</u>						
Brain	--	--	--	--	--	--
Thymus and Mediastinum	--	--	--	--	--	--
Thyroid Gland	--	--	--	--	--	--
Bronchus and Lung	--	--	--	--	--	--
Colon and Rectum	--	--	--	--	--	--
Kidney and Bladder	--	--	ns	--	--	ns
Prostate	--	--	--	--	--	--
Testicles	--	ns	--	--	NS	--
Ill-Defined Sites	--	--	--	--	--	--
Carcinoma In Situ of Penis	--	--	--	--	--	--
Carcinoma In Situ of Other and Unspecified Sites	--	--	--	--	--	--
Hodgkin's Disease	--	--	--	--	--	--
Leukemia	--	--	--	--	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	--	--	--	--	--	ns
Skin and Systemic Neoplasms						
All	NS	ns	ns	NS	ns	NS

+: C*T: Relative risk for ≤18.6 category less than relative risk for >18.6 category.

≤18.6 and >18.6: Relative risk 1.00 or greater.

-.: ≤18.6 and >18.6: Relative risk less than 1.00.

NS/ns: Not significant (p>0.10).

NS*/ns*: Marginally significant (0.05<p≤0.10).

-.: Analysis not performed due to sparse data.

Note: P-value given if p≤0.05.

A capital "NS" denotes relative risk for ≤18.6 category less than relative risk for >18.6 category or relative risk 1.00 or greater. A lowercase "ns" denotes relative risk for ≤18.6 category greater than relative risk for >18.6 category or relative risk less than 1.00.

TABLE 7-21. (Continued)

Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	C*T	Minimal		Adjusted		
		≤18.6	>18.6	C*T	≤18.6	>18.6
Skin Neoplasms						
<u>Behavior</u>						
All	NS	ns*	ns	NS	ns	NS
Malignant	NS	ns	ns	NS	ns	ns
Benign (Non-Blacks only)	NS	ns	ns	NS	ns	NS
Benign (Blacks Included)	NS	ns	ns	NS	ns	NS
Uncertain Behavior or Unspecified Nature	--	--	--	--	--	--
<u>Cell Type</u>						
Basal Cell Carcinoma						
All Sites Combined	NS	ns	ns	NS	ns	ns
Ear, Face, Head, and Neck	ns	ns	-0.047	ns	ns	ns
Trunk	ns	NS	NS	ns	NS	NS
Upper Extremities	--	--	--	--	--	ns
Lower Extremities	--	--	--	--	--	--
Other Sites and NOS	--	--	NS	--	--	NS
Sun Exposure-Related Malignant Skin Neoplasms						
All Sites Combined	NS	ns	ns	NS	ns	ns
Ear, Face, Head, and Neck	ns	ns	ns	ns	ns	ns
Trunk	ns	ns	ns	ns	NS	NS
Upper Extremities	--	--	--	--	--	ns
Lower Extremities	--	--	--	--	--	--
Other Sites and NOS	--	--	NS	--	--	NS

TABLE 7-21. (Continued)

Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	C*T	Minimal		Adjusted		
		≤18.6	>18.6	C*T	≤18.6	>18.6
Melanoma						
All Sites Combined	--	--	--	--	--	--
Ear, Face, Head, and Neck	--	--	--	--	--	--
Trunk	--	--	--	--	--	--
Upper Extremities	--	--	--	--	--	--
Lower Extremities	--	--	--	--	--	--
Other Sites and NOS	--	--	--	--	--	--
Squamous Cell Carcinoma	--	--	--	--	--	--
<u>Basal Cell Carcinoma by Occupation</u>						
Officer - Ear, Face, Head, and Neck vs. None	NS	ns	ns	NS	NS	NS
Officer - Other Sites vs. None	--	--	--	NS	ns	ns
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	--	NS	--	--	ns	--
Enlisted Flyer - Other Sites vs. None	+0.017	NS	NS*	+0.027	NS	NS*
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	NS	ns*	ns	NS	ns*	ns
Enlisted Groundcrew - Other Sites vs. None	NS	ns	ns	NS	ns	ns

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	Minimal			Adjusted			Maximal		
	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6	C*T	≤18.6	>18.6
<u>Sun Exposure-Related</u>									
<u>Malignant Skin</u>									
<u>Neoplasm by Occupation</u>									
Officer -									
Ear, Face, Head, and									
Neck vs. None	NS	ns	ns	ns	NS	ns	NS	ns	ns
Officer -									
Other Sites vs. None	--	--	--	NS	ns	ns	NS	ns	ns
Enlisted Flyer -									
Ear, Face, Head, and									
Neck vs. None	--	NS	--	--	ns	--	--	ns	--
Enlisted Flyer -									
Other Sites vs. None	+0.017	NS	NS*	+0.026	NS	NS*	+0.026	NS	NS*
Enlisted Groundcrew -									
Ear, Face, Head, and									
Neck vs. None	NS	ns*	ns	NS	ns	ns	NS	ns	ns
Enlisted Groundcrew -									
Other Sites vs. None	NS	ns	ns	NS	ns	ns	NS	ns	ns
<u>Basal Cell Carcinoma</u>									
<u>(Number)</u>									
One vs. None	NS	ns	ns	ns	ns	ns	NS	ns	ns
Multiple vs. None	ns	ns	ns	NS	ns	ns	NS	ns	ns
<u>Systemic Neoplasms</u>									
All	NS	NS	NS	ns	+0.036	NS*	NS	+0.036	NS*
Malignant	ns	ns	ns	ns	NS	ns	NS	NS	ns
Benign	NS	NS	+0.026	NS	+0.030	+0.003	NS	+0.030	+0.003
Uncertain Behavior									
or Unspecified Nature	--	--	--	--	--	--	--	--	--
<u>Malignant Systemic Neoplasms</u>									
<u>by Location/Site</u>									
Ear, Face, Head, and									
Neck	--	--	--	--	--	--	--	--	--
Oral Cavity, Pharynx,									
and Larynx	--	--	--	--	--	--	--	--	--

TABLE 7-21. (Continued)

Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)

Variable	C*T	Adjusted		C*T	Maximal	
		Minimal			Minimal	Maximal
		≤18.6	>18.6		≤18.6	>18.6
<u>Malignant Systemic Neoplasms</u>						
<u>by Location/Site (continued)</u>						
Brain	--	--	--	--	--	--
Thymus and Mediastinum	--	--	--	--	--	--
Thyroid Gland	--	--	--	--	--	--
Bronchus and Lung	--	--	--	--	--	--
Colon and Rectum	--	--	--	--	--	--
Kidney and Bladder	--	--	ns	--	--	ns
Prostate	--	--	--	--	--	--
Testicles	--	--	--	--	--	--
Ill-Defined Sites	--	--	--	--	--	--
Carcinoma In Situ of Penis	--	--	--	--	--	--
Carcinoma In Situ of Other and Unspecified Sites	--	--	--	--	--	--
Hodgkin's Disease	--	--	--	--	--	--
Leukemia	--	--	--	--	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	--	--	--	--	--	--
Skin and Systemic Neoplasms						
All	NS	ns	NS	NS	NS	NS

+: C*T: Relative risk for ≤18.6 category less than relative risk for >18.6 category.

≤18.6 and >18.6: Relative risk 1.00 or greater.

-.: ≤18.6 and >18.6: Relative risk less than 1.00.

NS/ns: Not significant (p>0.10).

NS*/ns*: Marginally significant (0.05<p≤0.10).

-.: Analysis not performed due to sparse data.

Note: P-value given if p≤0.05.

A capital "NS" denotes relative risk for ≤18.6 category less than relative risk for >18.6 category or relative risk 1.00 or greater. A lowercase "ns" denotes relative risk for ≤18.6 category greater than relative risk for >18.6 category or relative risk less than 1.00.

TABLE 7-22.

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted			
			Unknown versus Background	Low versus Background	High versus Background	
Skin Neoplasms						
<u>Behavior</u>						
All	V	NS	NS*	NS	ns	
	VS	NS	NS*	NS	ns	
Malignant	V	NS	NS	NS	ns	
	VS	NS	NS	NS	ns	
Benign (Non-Blacks only)	V	NS	NS	NS	NS	
Benign (Blacks Included)	V	NS	NS	NS	NS	
Uncertain Behavior or Unspecified Nature	V	--	NS	--	--	
	VS	--	NS	ns	ns	
<u>Cell Type</u>						
Basal Cell Carcinoma						
All Sites Combined	V	NS	NS	NS	ns	
Ear, Face, Head, and Neck	V	0.019	NS	NS	-0.032	
Trunk	V	NS	NS	NS	NS	
Upper Extremities	V	NS	NS	NS	ns	
Lower Extremities	V	--	--	--	--	
Other Sites and NOS	V	0.011	ns	NS*	NS	

TABLE 7-22. (Continued)

Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Unadjusted			
			Unknown versus Background	Low versus Background	High versus Background	
Sun Exposure-Related Malignant Skin Neoplasms						
All Sites Combined	V	NS	NS	NS	ns	
Ear, Face, Head, and Neck	V	0.026	NS	NS	-0.050	
Trunk	V	NS	NS	ns	NS	
Upper Extremities	V	NS	NS	NS	NS	
Lower Extremities	V	--	--	--	--	
Other Sites and NOS	V	0.011	ns	NS*	NS	
Melanoma						
All Sites Combined	V	--	ns	ns	ns	
Ear, Face, Head, and Neck	V	--	NS	--	--	
Trunk	V	--	ns	ns	ns	
Upper Extremities	V	--	--	--	--	
Lower Extremities	V	--	--	--	--	
Other Sites and NOS	V	--	--	--	--	
Squamous Cell Carcinoma	V	NS	NS	NS	NS	

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Basal Cell Carcinoma by Occupation</u>					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Officer - Other Sites vs. None	V	NS	NS	NS	ns
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	0.003	ns	NS	+0.020
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	NS*	NS	NS	ns*
Enlisted Groundcrew - Other Sites vs. None	V	NS*	ns	NS	ns
<u>Sun Exposure-Related Malignant Skin Neoplasm by Occupation</u>					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Officer - Other Sites vs. None	V	NS	NS	NS	ns

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Sun Exposure-Related Neoplasms by Occupation (continued)</u>					
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	0.010	ns	NS	+0.049
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	NS	NS	NS	ns
Enlisted Groundcrew - Other Sites vs. None	V	NS*	ns	NS	ns
<u>Basal Cell Carcinoma (Number)</u>					
One vs. None	V	NS	NS	NS	ns
Multiple vs. None	V	NS*	NS*	NS	ns
Systemic Neoplasms					
All	V	NS*	ns*	NS	NS
	VS	NS*	ns*	NS	NS
Malignant	V	0.001	ns	+0.016	ns
Benign	V	0.044	ns	ns	+0.043
Uncertain Behavior or Unspecified Nature	V	NS	ns	ns	ns
	VS	NS	ns	ns	ns

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Malignant Systemic Neoplasms by Location/Site</u>					
Ear, Face, Head, and Neck	V	--	ns	ns	ns
Oral Cavity, Pharynx, and Larynx	V	--	ns	ns	ns
Brain	V	--	--	--	--
Thymus and Mediastinum	V	--	NS	--	--
Thyroid Gland	V	--	--	--	--
Bronchus and Lung	V	--	NS	NS	--
Colon and Rectum	V	--	ns	ns	ns
Kidney and Bladder	V	0.006	NS	+0.033	ns
Prostate	V	--	ns	NS	ns
Testicles	V	--	--	NS*	--
Ill-Defined Sites	V	--	--	--	--
Carcinoma In Situ of Penis	V	--	ns	ns	ns
Carcinoma In Situ of Other and Unspecified Sites	V	--	--	--	--
Hodgkin's Disease	V	--	ns	ns	ns
Leukemia	V	--	--	NS	--

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Malignant Systemic Neoplasms by Location/Site (continued)</u>					
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	V	NS	NS	NS	ns
Skin and Systemic Neoplasms					
All	V VS	NS NS	NS NS	NS NS	NS NS

+: Relative risk 1.00 or greater.

-: Relative risk less than 1.00.

V: Verified neoplasms only.

VS: Verified and suspected neoplasms.

NS/ns: Not significant ($p > 0.10$).

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

--: Analysis not performed due to sparse data.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00; a capital "NS" under the "All" column does not imply directionality.

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
Skin Neoplasms					
<u>Behavior</u>					
All	V	NS	NS	NS	ns
	VS	NS	NS	NS	ns
Malignant	V	NS	NS	NS	ns
	VS	NS	NS	NS	ns
Benign (Non-Blacks only)	V	NS	NS	NS	NS
Benign (Blacks Included)	V	NS	NS	NS	NS
Uncertain Behavior or Unspecified Nature	V	--	--	--	--
	VS	--	--	--	--
<u>Cell Type</u>					
Basal Cell Carcinoma					
All Sites Combined	V	NS	NS	NS	ns
Ear, Face, Head, and Neck	V	NS*	NS	NS	ns*
Trunk	V	NS	NS	NS	NS
Upper Extremities	V	NS	NS	NS	--
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	0.035	--	+0.024	NS

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
Sun Exposure-Related Malignant Skin Neoplasms					
All Sites Combined	V	NS	NS	NS	ns
Ear, Face, Head, and Neck	V	NS	NS	NS	ns
Trunk	V	NS	NS	ns	NS
Upper Extremities	V	NS	NS	NS	NS
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	0.035	--	+0.024	NS
Melanoma					
All Sites Combined	V	--	ns	--	--
Ear, Face, Head, and Neck	V	--	--	--	--
Trunk	V	--	--	--	--
Upper Extremities	V	--	--	--	--
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	--	--	--	--
Squamous Cell Carcinoma	V	NS	NS	NS	NS

TABLE 7-22. (Continued)

Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Basal Cell Carcinoma by Occupation</u>					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	--
Officer - Other Sites vs. None	V	NS	NS*	NS	--
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	0.028	--	NS	+0.017
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	0.048	NS	NS	ns
Enlisted Groundcrew - Other Sites vs. None	V	NS*	--	NS	ns
<u>Sun Exposure-Related Malignant Skin Neoplasm by Occupation</u>					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	--
Officer - Other Sites vs. None	V	NS	NS	NS	--

TABLE 7-22. (Continued)
Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Sun Exposure-Related Malignant Skin Neoplasm by Occupation (continued)</u>					
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	NS*	--	NS	+0.028
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	NS	NS	NS	ns
Enlisted Groundcrew - Other Sites vs. None	V	NS*	--	NS	ns
<u>Basal Cell Carcinoma (Number)</u>					
One vs. None	V	NS	NS	NS	ns
Multiple vs. None	V	NS*	+0.039	+0.038	ns
Systemic Neoplasms					
All	V	0.021	ns*	NS	NS*
	VS	0.022	-0.050	NS	NS*
Malignant	V	0.002	ns	+0.004	--
Benign	V	0.011	ns	ns	+0.010
Uncertain Behavior or Unspecified Nature	V	NS	ns	ns	ns
	VS	NS	ns	ns	ns

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Malignant Systemic Neoplasms by Location/Site</u>					
Ear, Face, Head, and Neck	V	--	--	--	--
Oral Cavity, Pharynx, and Larynx	V	--	--	--	--
Brain	V	--	--	--	--
Thymus and Mediastinum	V	--	--	--	--
Thyroid Gland	V	--	--	--	--
Bronchus and Lung	V	--	--	--	--
Colon and Rectum	V	--	--	--	--
Kidney and Bladder	V	0.041	NS	+0.014	--
Prostate	V	--	--	NS	--
Testicles	V	--	--	--	--
Ill-Defined Sites	V	--	--	--	--
Carcinoma In Situ of Penis	V	--	--	--	--
Carcinoma In Situ of Other and Unspecified Sites	V	--	--	--	--
Hodgkin's Disease	V	--	--	--	--
Leukemia	V	--	--	--	--
Other Malignant Neoplasms of Lymphoid and and Histiocytic Tissue	V	NS	NS	NS	--

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
Skin and Systemic Neoplasms					
All	V	NS	NS	NS	NS
	VS	NS	NS	NS	NS

-: Relative risk less than 1.00.

+: Relative risk 1.00 or greater.

V: Verified neoplasms only.

VS: Verified and suspected neoplasms.

NS/ns: Not significant ($p > 0.10$).

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

--: Analysis not performed due to sparse data.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00; a capital "NS" under the "All" column does not imply directionality.

Skin Neoplasm Analyses

As shown in Table 7-1, the frequency of participants with skin neoplasms were evaluated from several different perspectives: behavior (i.e., malignant, benign, uncertain behavior or unspecified nature), cell type (i.e., basal cell or squamous cell carcinoma, melanoma, and sun exposure-related malignant skin neoplasm), cell type by specified anatomical location/site, and cell type and specified anatomical location/site by occupation.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In general, the various analyses of the frequency of Ranch Hands having skin neoplasms did not indicate a positive association with initial dioxin. For the most part, the relative risks estimated from the unadjusted and adjusted models were less than 1 and nonsignificant. When significant or marginally significant relative risks were found they were usually less than 1. Significant relative risks greater than 1 were found in the occupation-specific analyses comparing the frequencies of Ranch Hand enlisted flyers with a basal cell carcinoma of other sites versus those Ranch Hand enlisted flyers without a basal cell carcinoma (unadjusted analysis: $p=0.050$ for the minimal assumption, $p=0.015$ for the maximal assumption; adjusted analysis: $p=0.039$ for maximal assumption). Significant or marginally significant relative risks greater than 1 were also found in the corresponding analyses of Ranch Hand enlisted flyers for sun exposure-related malignant skin neoplasms of other sites versus no sun exposure-related malignant skin neoplasm (unadjusted analysis: $p=0.052$ for minimal assumption, $p=0.015$ for maximal assumption; adjusted analysis: $p=0.049$ for maximal assumption). The comparable analyses for the other occupational groups had relative risks less than 1. These inconsistent results suggest that other factors may be involved in this increase in skin malignancy among enlisted flyers. Only a limited number of analyses for melanoma were performed due to sparse data.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

In general, the unadjusted and the adjusted analyses of the various skin neoplasm variables found few significant interactions between current dioxin and time since tour. There were individual time strata with significant or marginally significant relative risks; the risks, in general, however, were less than 1. Similar to the analyses involving initial dioxin, Ranch Hand enlisted flyers with a basal cell carcinoma of other sites when contrasted with Ranch Hand enlisted flyers without a basal cell carcinoma displayed significant current dioxin-by-time interactions ($p<0.030$ for unadjusted and adjusted analyses under both assumptions). In both the unadjusted and the adjusted analyses, the relative risks were greater than 1 in each time stratum and were significant ($p<0.040$ for the unadjusted analysis under each assumption) or marginally significant ($p<0.060$ for the adjusted analysis under each assumption) for those Ranch Hand enlisted flyers with earlier tours (i.e., time since tour over 18.6 years). Corresponding analyses of Ranch Hand enlisted flyers with a sun exposure-related malignant skin neoplasm of other sites versus Ranch Hand enlisted flyers without a sun exposure-related malignant skin neoplasm also contained significant interactions between current dioxin and time and a relative risk greater than 1 in each time stratum. Ranch Hands in the earlier time stratum had a significant or marginally significant relative risk. As with the analysis using initial dioxin, only a limited number of analyses were performed for melanoma because of sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In general, the unadjusted and adjusted analyses for all skin neoplasms, all malignant skin neoplasms, benign skin neoplasms, and all skin neoplasms of uncertain behavior or unspecified nature exhibited nonsignificant overall and individual contrasts among Ranch Hands in the three current dioxin categories and the Comparisons in the background category. With the exception of the high versus background contrast for all skin neoplasms and the high versus background contrast for all malignant skin neoplasms, most of the individual Ranch Hand versus Comparison contrasts displayed relative risks that were greater than 1 and nonsignificant. For the high versus background contrasts of these analyses, the relative risks were less than 1 and nonsignificant.

The unadjusted and adjusted analyses for basal cell carcinoma of the ear, face, head, and neck exhibited significant ($p=0.019$) and marginally significant ($p=0.087$) overall contrasts, respectively. In the unadjusted analysis, the high versus background contrast had a relative risk significantly less than 1 ($p=0.032$). In the adjusted analysis, the relative risk for the high versus background contrast was less than 1 and marginally significant ($p=0.063$). The unadjusted analysis for sun exposure-related malignant skin neoplasms of the ear, face, head, and neck also exhibited a significant overall contrast ($p=0.026$) and a relative risk for the high versus background contrast that was less than 1 and significant ($p=0.050$); however, the adjusted analysis was not significant.

The unadjusted and adjusted analyses for basal cell carcinoma of other sites and sites NOS exhibited significant overall contrasts of the three Ranch Hand current dioxin categories and the Comparison background category ($p=0.011$ and $p=0.035$, respectively). The unadjusted and adjusted analyses had relative risks greater than 1 associated with the low versus background contrasts that were marginally significant ($p=0.053$) and significant ($p=0.024$), respectively. The other contrasts were nonsignificant.

In general, there was a sparse number of participants with melanoma. Therefore, only a limited number of analyses could be performed and no significant contrasts or relative risks were noted.

The unadjusted and the adjusted analyses exhibited significant overall contrasts for enlisted flyers with a basal cell carcinoma of other sites ($p=0.003$ and $p=0.028$, respectively). The high versus background contrast displayed a significant relative risk that was greater than 1 in the unadjusted analysis ($p=0.020$) and in the adjusted analysis ($p=0.017$). The analyses for the enlisted groundcrew contained significant or marginally significant overall contrasts; however, the associated Ranch Hand versus Comparison contrasts were usually nonsignificant. Enlisted flyers with a sun exposure-related malignant skin neoplasm of other sites also exhibited at least marginally significant overall contrasts and significant high versus background contrasts with relative risks greater than 1.

In the unadjusted and adjusted analyses for participants with multiple basal cell carcinoma versus no basal cell carcinoma, there were marginally significant overall contrasts in the unadjusted analysis ($p=0.053$) and the adjusted analysis ($p=0.078$). The unknown versus background contrast displayed a relative risk greater than 1 that was marginally significant in the unadjusted analysis ($p=0.060$) and significant in the adjusted analysis

($p=0.039$). In the unadjusted analyses, the relative risk for the low versus background contrast was greater than 1 but nonsignificant. The adjusted relative risk for this contrast was greater than 1 and significant ($p=0.038$). The high versus background contrasts had nonsignificant relative risks that were less than 1.

Systemic Neoplasm Analyses

As Table 7-1 shows, the frequency of participants with systemic neoplasms were evaluated for two different characteristics: behavior and location/site.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

For both the unadjusted and the adjusted analyses of all systemic neoplasms (benign and malignant combined), significant relative risks greater than 1 were found under the maximal assumption ($p=0.009$ and $p=0.006$, respectively) and nonsignificant relative risks greater than 1 were found under the minimal assumption. The unadjusted analysis of Ranch Hands with a malignant systemic neoplasm under the minimal assumption yielded a relative risk less than 1 that was significant ($p=0.048$) with the relative risks from the other analyses also being less than 1 but nonsignificant. The unadjusted and the adjusted relative risks for Ranch Hands with a benign systemic neoplasm were significant and greater than 1 in both the minimal analysis ($p=0.022$ and $p=0.015$, respectively) and the maximal analysis ($p=0.001$ and $p<0.001$, respectively). In these analyses, the benign systemic neoplasms were predominantly lipomas (approximately 75 percent); also found, but with less frequency, were hemangiomas, dermoid cysts, fibromas, benign adenolymphoma, neurofibroma, facial fibroma, and adenoma. The unadjusted and adjusted analyses of the frequency of Ranch Hands with a systemic neoplasm of uncertain behavior or unspecified nature yielded nonsignificant relative risks.

For the most part, unadjusted and adjusted analyses of the systemic neoplasms could not be performed by location/site due to the sparse number of Ranch Hands with a systemic neoplasm at an individual location/site. For the few location/sites for which analyses were performed (kidney and bladder, prostate, testicles, and other malignant neoplasms of lymphoid and histiocytic tissue), the relative risks were nonsignificant.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

The unadjusted and adjusted analyses of the frequency of Ranch Hands with systemic neoplasms (benign and malignant combined) exhibited nonsignificant interactions between current dioxin and time since tour. However, marginally significant relative risks greater than 1 were found under the maximal assumption (unadjusted, $p=0.098$; adjusted, $p=0.065$) for Ranch Hands with earlier tours (over 18.6 years). In the adjusted analysis, a significant relative risk greater than 1 ($p=0.036$) was found under the maximal assumption for Ranch Hands with later tours (i.e., 18.6 years or less).

For Ranch Hands with malignant systemic neoplasms, the interactions between current dioxin and time since tour were nonsignificant regardless of the analysis or assumption.

For Ranch Hands with benign systemic neoplasms, the interactions between current dioxin and time since tour were nonsignificant. However, under the minimal assumption, the

unadjusted and adjusted analyses for Ranch Hands with earlier tours exhibited significant relative risks greater than 1 ($p=0.035$ and $p=0.026$, respectively). Under the maximal assumption, the unadjusted analysis displayed a relative risk that was greater than 1 and marginally significant for Ranch Hands with later tours ($p=0.095$) and a relative risk greater than 1 and significant for Ranch Hands with earlier tours ($p=0.013$). In the adjusted analysis under the maximal assumption, the relative risks of both time strata were greater than 1 and significant (≤ 18.6 years, $p=0.030$; ≥ 18.6 years, $p=0.003$).

In general, the analyses by site of the frequency of Ranch Hands with a systemic neoplasm were limited because of the sparse number of Ranch Hands with a systemic neoplasm at a specified site/location.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis for Ranch Hands with a systemic neoplasm, the overall contrast of Ranch Hands in the three current dioxin categories and Comparisons in the background category was marginally significant ($p=0.087$); the relative risk for the unknown versus background contrast was less than 1 and also marginally significant ($p=0.072$). The other Ranch Hand versus Comparison contrasts had relative risks greater than 1 that were nonsignificant. The corresponding adjusted analyses contained a significant overall contrast ($p=0.021$), a relative risk for the unknown versus background contrast that was less than 1 and marginally significant ($p=0.057$), and a high versus background contrast with a marginally significant relative risk greater than 1 ($p=0.072$). The adjusted relative risk for the low versus background contrast was greater than 1 but nonsignificant. After including participants with suspected neoplasms in the analysis, similar results were produced.

The unadjusted and adjusted analyses for malignant systemic neoplasms indicated that the overall contrast of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category was significant ($p=0.001$ and 0.002 , respectively). The low versus background contrast had significant relative risks greater than 1 in the unadjusted analysis ($p=0.016$) and in the adjusted analysis ($p=0.004$). No Ranch Hands in the high current dioxin category had a malignant systemic neoplasm. The unknown versus background contrasts were nonsignificant.

For benign systemic neoplasms, the unadjusted and the adjusted analyses displayed significant overall contrasts among Ranch Hands in the three current dioxin categories and Comparisons in the background category ($p=0.044$ and $p=0.011$, respectively). The high versus background contrast exhibited a significant relative risk greater than 1 in the unadjusted analysis ($p=0.043$) and in the adjusted analysis ($p=0.010$).

For systemic neoplasms of uncertain behavior or unspecified nature, the overall contrast and individual Ranch Hand versus Comparison contrasts were nonsignificant in the unadjusted and the adjusted analyses.

In general, the analyses by site of the frequency of participants with a systemic neoplasm were limited because of the sparse numbers. The unadjusted and adjusted analyses of participants with a malignant systemic neoplasms of the kidney and bladder produced significant overall contrasts among the three Ranch Hand current dioxin categories

and the Comparison background category ($p=0.006$ and $p=0.041$, respectively). The low versus background contrast exhibited a significant relative risk greater than 1 in the unadjusted analysis ($p=0.033$) and in the adjusted analysis ($p=0.014$). No Ranch Hands in the high current dioxin category had a malignant systemic neoplasm of the kidney and bladder. The unknown versus background contrasts were nonsignificant.

Skin and Systemic Neoplasm Analysis

As Table 7-1 displays, study participants with either a skin or a systemic neoplasm were combined for analysis to investigate the association with initial dioxin, current dioxin and time since tour, and categorized current dioxin.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

The unadjusted and adjusted analyses of the frequency of Ranch Hands with a skin or systemic neoplasm produced nonsignificant relative risks.

Model 2: Ranch Hands - Log₂ (Current Dioxin) and Time

Under each assumption, the unadjusted analysis and adjusted analysis of the frequency of Ranch Hands with a skin neoplasm or a systemic neoplasm displayed nonsignificant interactions between current dioxin and time since tour.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted and adjusted analyses of participants with a skin or a systemic neoplasm indicated that the overall contrast of the three Ranch Hand current dioxin categories and the Comparison background category was nonsignificant, as were the individual Ranch Hand versus Comparison contrasts.

CONCLUSION

In summary, the analyses generally did not establish a significant positive association between dioxin and the presence of skin neoplasms. Significant relative risks were found for the skin neoplasm analyses; however, the relative risks were almost always less than 1. For the analyses focusing on enlisted flyers with a basal cell carcinoma of other sites (and sun exposure-related malignant skin neoplasms of other sites), relative risks were found to be significant and greater than 1. However, these results may be the result of a multiple-testing artifact, since they were not noted for the enlisted groundcrew who, as a group, had higher levels of serum dioxin than the enlisted flyers.

In general, the analyses using all systemic neoplasms combined produced some significant or marginally significant relative risks greater than 1. However, after performing the analyses separately by behavior (malignant neoplasms, benign neoplasms, and neoplasms of uncertain behavior and unspecified nature), the analyses of participants with a benign systemic neoplasm, such as lipomas, were found to have significant relative risks greater than 1 in contrast to the nonsignificant relative risks, which were often less than 1, for participants with a malignant systemic neoplasm.

The study provides no evidence of increased incidence for the neoplasms most commonly suspected as being associated with exposure to chlorophenols (HD, NHL, and

STS). However, the number of participants with these specific neoplasms was small; therefore, the statistical power to detect small or moderately elevated relative risks was low. There is no evidence in these data of a relationship between dioxin and either skin or systemic cancer. There is a suggestion of a dose-related relationship between dioxin and benign systemic neoplasms (lipomas) that will be explored in greater depth in the 1992 physical examination.

CHAPTER 7

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